VARIATION IN NHS UTILISATION OF VAULT CYTOLOGY TESTS IN WOMEN POST-HYSTERECTOMY

by

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A thesis submitted to the Faculty of Medicine of
The University of Birmingham
for the degree of
DOCTOR OF PHILOSOPHY

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December 2009

ABSTRACT

Hysterectomy is commonly performed but there is scant evidence concerning appropriate follow-up by vaginal vault cytology testing.

This observational, retrospective cohort study, using routinely collected data, linked women's entire cervical screening histories with their operation details and subsequent vault cytology test results, to establish: Which women are having hysterectomies? What was the indication? Which were followed-up? How did they differ from those who were not?

6,141 women underwent hysterectomy; an incidence of 23/10,000 women/pa. 11.61% had malignancy, 3% had CIN and 82.9% had benign disease. Median age was 48 years, women were of greater deprivation and different ethnicity from the background population.

Post-operatively 1,016 (16.5%) had vault cytology testing. Those having CIN at total hysterectomy should have vault cytology but only 63% had any, of these less than 10% had it according to protocol.

Many factors were associated with having vault cytology (younger, less deprived, non-benign diagnosis and abnormal index cytology) but few clinically meaningful. Only 2.9% of vault cytology tests were abnormal.

Efforts to identify and eradicate inappropriate use of vault tests should swiftly lead to savings. Although national guidelines are targeting the right women, it is recommended that all vaginal vault cytology should be undertaken in secondary care hereafter.

ACKNOWLEDGEMENTS

I would like to sincerely thank the following people and organisations, without their support this research and dissertation would not have been possible:

***Professor Sue Wilson**, my mentor and supervisor for the past nine years, her guidance, wisdom, pragmatism and humour have been both inspirational and stabilising. I will always be indebted to her.*

***Dr John Macleod**, my superb PhD supervisor, his unfailing support, understanding and positive encouragement have been invaluable.*

***The National Co-ordinating Centre for Research Capacity Development**, for funding my research so generously via a Researcher Development Award.*

***The Department of Primary Care and General Practice**, particularly Professor Richard Hobbs, for having the insight to value Academic General Practice and the belief to fight for the resources to fund training schemes.*

***Roger Holder, Sayeed Haque and Andrea Roalfe,** for providing guidance and personal statistics tuition.*

***Christine Waddell and Linda Bentley** from Birmingham Women's Hospital Cytopathology Department, for their encouragement and support.*

***The Cloisters Medical Practice staff** for their forbearance and understanding*

***The data providers:** HES who, despite considerable difficulties following loss of their headquarters in Hemel Hempstead, managed to generate my data. The ten Exeter database managers, Philippa Pearmain, Helen Bagnall and Justin Askew at WMQARC and the 19 hospitals of the region who undertake gynaecological surgery. In particular the staff of Good Hope, Heartlands, Hereford and Birmingham Women's Hospital laboratories for access to their data.*

***Dr Julie Best**, my great friend and 'sounding board', for taking the time to read and comment on the draft.*

***Dad** for always believing in me and encouraging every adventure I contemplate, however ambitious or outrageous, and for being the most amazing role model.*

***Mum** for her unsurpassed love, generosity and calming, stabilising influence throughout my life. In particular I thank her for the many hours she spent diligently proof reading this dissertation.*

***Paul**, for understanding why I had to do a PhD, supporting me throughout and for being my best friend through the good times and the bad. Here's to our next adventure…*

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LIST OF ABBREVIATIONS

ACC	Accredited Clinical Coder
ACCESS	Relational database computer package
A&E	Accident and Emergency Department
BWH	Birmingham Women's NHS Foundation Trust
CC	Clinical Coding
CfH	NHS Connecting for Health
CI	Confidence Interval - a statistical term, whereby a CI of 95% means the confidence interval around an estimate.+/- 2 standard deviations
CIN	Cervical Intraepithelial Neoplasia
CSD	Cegedim Strategic Data
CSV	Comma Separated Variable file
DGH	District General Hospital
DoH	Department of Health
DPA98	Data Protection Act 1998
THIN	The Health Improvement Network (database)
Excel	Spreadsheet computer package
Exeter	NSHIA computer database network used to manage all the data concerning patient registrations with GPs and screening data.
GP	General Practitioner
GPRD	General Practice Research Database
GSS	Government Statistical Service
ICD	International Classification of Disease (9 or 10 denotes which edition)
H&SCA	Health and Social Care Act
HES	Hospital Episode Statistics
HIS	Health Informatics Service
HSE	Health Survey for England
HPV	Human Papilloma Virus
ICD 10	International Classification of Diseases, 10th edition.
IHTSDO	International Health Terminology Standards Development Organisation
IUCD	Intrauterine contraceptive device (also known as a contraceptive coil)
KS	Key Statistics
N/A	Not applicable
NAO	National Audit Office
NCCRCD	National Coordinating Centre for Capacity Development
NCRS	National Care Records Service
NHS	National Health Service
NHSCSP	National Health Service Cervical Screening Programme
NHAIS	National Health Applications and Infrastructure Services
NHSIA	National Health Service Information Authority
NIGB	National Information Governance Board for Health and Social Care
NPfIT	National Programme for IT
NPSA	National Patient Safety Agency
NSTS	NHS Strategic Tracing Service
OPCS	Office of Population Censuses and Surveys - merged 1996 with Central Statistical Offices to form the Office for National Statistics
OCPS-4	UK Classification of Operative Procedures
ONS	Office for National Statistics (see above)
p value	probability value

Pap test	Papanicolaou test for cellular changes in the cervical tissue
PCO	Primary Care Organisation
PCT	Primary Care Trust
PhD	Doctor of Philosophy
PIAG	Patient Information Advisory Group
RCGP	The Royal College of General Practitioners
RCOG	The Royal College of Obstetricians and Gynaecologists
SHA	Strategic Health Authority
SCAG	Security and Confidentiality Advisory Group of HES
SPSS	Statistical computer package designed for Social Sciences research
SNOMED	Systemised Nomenclature of Medicine
SNOMED CT	SNOMED Clinical Terms subset
UK	United Kingdom
UKTC	UK Terminology Centre
USA	United States of America
VIN	Vulval Intraepithelial Neoplasia
VaIN	Vaginal Intraepithelial Neoplasia
WHO	World Health Organization

CHAPTER ONE: INTRODUCTION

In the United Kingdom, around 20% of the female population undergo surgical removal of the uterus during their lifetime.[1,2] This major operation is known as a 'hysterectomy'. Over 98% women who have their uterus surgically removed also have the cervix uteri or 'neck' of the uterus removed at the same time, a 'total hysterectomy',[3] this leaves the vagina as a pouch with a blind end at the site of amputation of the cervix, the 'vaginal vault'. This thesis will consider data on a cohort of women who have had a hysterectomy operation and whether or not they are followed up after surgery by cytological screening of the vaginal vault.

There are now several effective and less invasive alternatives to hysterectomy available to women and their Gynaecologists[4]; however, approximately 38,000 hysterectomy procedures were undertaken in England in 2007-8 (most recent data) and 600,000 in the USA, making it one of the most frequently performed major surgical procedures.[5;6] Over 90% of hysterectomy operations are known to be performed for benign indications,[7] such as the presence of fibroids and dysfunctional uterine bleeding (DUB).[4] The remaining operations are performed for removal of malignancies (endometrial, cervical, vaginal and ovarian), and additionally to remove Cervical Intraepithelial Neoplasia (CIN), a condition which may be a precursor to invasive cervical cancer.[8]

Even though it is performed often, hysterectomy is not without risk: a large cohort study (the VALUE study) recorded an operative complication rate of 3.5% and a post-operative complication rate of 9%, with 1% requiring a return trip to the operating theatre.[1] The Royal College of Obstetricians and Gynaecologists of the UK has estimated operative mortality from hysterectomy in the UK as being around one in 4,000 women.[9] These figures are significantly lower than those reported in other older studies.[10;11] This may reflect the fact that the 'VALUE' study was based upon self report by Gynaecologists and is not comprehensive; thus the study is believed to reflect around 45% of all hysterectomy operations in the UK from 1994 to 1995, alternatively the situation has substantially improved over time.

Previously it had been noted that an inverse gradient in social class and incidence of hysterectomy existed, in the UK,[2;12] meaning that as women become more deprived their risk of undergoing hysterectomy increases.[13;14] However, it is not known if this social class gradient persists with respect to follow-up. Several large cohort studies have examined the indications for hysterectomy in the UK, however none has published any details of subsequent follow-up by means of the vaginal vault cytology test.[1;2]

Total hysterectomy is usually a reason for ceasing routine cervical screening as the cervix is no longer present. The aim of the UK National Health Service Cervical Screening Programme (NHSCSP) is to prevent cervical cancer, however, it does offer some guidance about use of vault testing post-hysterectomy.[15,16]

No international consensus exists on the appropriate cytological screening in women who have undergone a total hysterectomy, as evidence for the appropriate use of vaginal vault cytology tests (vault smears) post-hysterectomy and the optimum period of follow-up is sparse. Cervical smear tests are known to cause anxiety to users and have a financial cost to the NHS.[17] There is no reason to presume that this does not also apply to vault smears also.

A vaginal vault cytology test or 'vault smear' is an exfoliative cytological sample taken from the blind end of the vagina in a similar way to the taking of a cervical Papanicolaou cytology test (See Chapter 2.3 for further explanation). The sample is stained and a slide produced in a Cytopathology laboratory according to standard procedures and this slide may be examined under a microscope and then 'classified' according to internationally agreed criteria.

The classification of vaginal vault cytology tests is based on the same classification system as cervical cytology tests, with suitable additions to describe vaginal abnormalities. The classification currently used is the British Society for Clinical Cytology (BSCC) and NHSCSP terminology.[18] Recommended follow-up by means of vault smear tests after hysterectomy depends upon histology results at the time of hysterectomy (Figure 1).

The majority of published studies in this area, recommend the use of vaginal cytology in the follow-up of women who have had a hysterectomy subsequent to the diagnosis of an invasive tumour of the cervix, or where invasive disease is an incidental finding at hysterectomy.[19-21] However, with respect to follow-up after hysterectomy for benign indications the literature is less clear.[22;23] A systematic review of the literature could not identify any robust data to establish the benefit and effectiveness of follow-up, by 'vault smears' or 'vault cytology', of women who have had a hysterectomy for benign indications (see Chapter 2.3.2 for further information).[24]

The available evidence does, however, suggest that the vaginal vault cytology test has a very low positive predictive value when used as a screening tool for the presence of residual abnormality after CIN in the absence of symptoms or clinical signs or for screening for Vaginal Intraepithelial Neoplasia (VaIN).[22;23;25] Therefore, most commentators recommend that the use of vault cytology tests for post-hysterectomy follow-up is only required for women who have had a histological diagnosis of CIN III or frank malignancy.[19-21] Even then, vaginal vault cytology tests should be limited to those who present with symptoms or in whom an abnormality is detected clinically.[26]

Half of all vault smear tests are conducted in the primary care setting in the UK but primary healthcare professionals' knowledge about the role of the test is poor,[27] professionals whose knowledge about the test was best, performed the test least often.[27]

Only one significant abnormality was detected in an audit of over 4,000 specimens taken in Primary Care[28] and vault smear tests in asymptomatic women can have a high false positive rate.[22] One American study compared the results of vault cytology tests with cervical cytology tests, in matched controls, and noted that there was a significantly reduced risk of test abnormality in those followed up post-hysterectomy.[29]

Figure 1 lists the current NHSCSP guidelines for appropriate use of vaginal vault cytology in the UK.[16]

Figure 1: Current national guidelines for the routine use of vaginal vault cytology[16]

"Women who have had a hysterectomy with CIN present are potentially at risk of developing vaginal intraepithelial neoplasia (VaIN) and invasive vaginal disease. There is no clear evidence that colposcopy increases the detection of disease on follow-up. Expert consensus opinion recommends that:

(i) for women on routine recall for at least 10 years prior to hysterectomy and no CIN in the sample at hysterectomy, no vault cytology is required.

(ii) for women with less that 10 years' routine recall and no CIN at hysterectomy, a sample should be taken from the vault six months after surgery and there should be no further cytology follow-up if it is negative.

(iii) for women with completely excised CIN at hysterectomy, a sample should be taken from the vault at six and 18 months after surgery and there should be no further cytology follow-up if both are negative.

(iv) for women with incomplete or uncertain excision of CIN follow-up should be conducted as if the cervix were still in situ (i.e. as for low and high risk follow-up).

It should be emphasised that these clinical guidelines for follow-up of women treated by hysterectomy are not part of the cervical screening programme and data on cytology from vault samples are not collected routinely."

Several large-scale national cohort studies have reported the socioeconomic distribution of patients undergoing hysterectomy[12] and distribution of hysterectomy type (vaginal versus abdominal).[1] However, no large, robust studies have been undertaken to establish actual patterns of follow-up, by means of vault smear tests, after hysterectomy. We do not have any recent representative data on variability in follow up; compliance with national guidelines is, at present, also unknown. Until we understand what actually is taking place, how much variability exists and why, it is difficult to suggest improvements, even though preliminary work suggests that vaginal vault cytology testing may be taking place inappropriately.[28]

No international consensus exists as to the most appropriate follow up by vault smear test after hysterectomy;[29] the UK guidelines that exist are not based upon robust 'gold-standard' evidence.[16] With increasing pressure on diagnostic and treatment services every year, the identification of inappropriate usage of and evaluation of diagnostic services is more important than ever. Thus there is a need for an adequately powered study to consider the issue of inappropriate use of vaginal vault cytology testing, the outcome of which may be used to inform national guidelines and encourage the teaching of best practice.

The research reported in this thesis intends to fill a void in current knowledge concerning which women undergo hysterectomy operations and why and then describing the appropriateness, or otherwise, of any subsequent follow up.

In future national guidelines should be truly evidence based so that clinicians may be better able to inform their patients about the benefits and costs of screening using vaginal vault cytology tests. To achieve this, a data linkage study of routinely collected datasets was undertaken and is now described in the forthcoming chapters:

- Chapter two explores the background literature; a summary of what is already known about hysterectomy, cervical screening, use of vault cytology testing and some information about the chosen study methodology.
- Chapter three explains the study methodology in detail, starting with the ethical approvals, then outlining the various data sources and concluding with the plan of data analysis.
- Chapter four outlines the processes involved in extracting the study data from the source material, linking the databases and then anonymising the data.
- Chapter five explains how the study data were validated and coded, in readiness for analysis.
- Chapter six describes the results of the study; starting with demographic data of the whole cohort, then looking at women's cervical screening histories, then considering what happened at hysterectomy and finally examining any subsequent follow-up by means of vaginal vault cytology.
- Chapter seven explores the results by discussing the whole project and examining the results and analysis, and attempting to explain the findings.
- Chapter eight includes the study conclusion and recommendations.

SUMMARY OF INTRODUCTORY CHAPTER

The aim of this study is to describe the variation in hysterectomy rates and any subsequent follow-up by use of the vaginal vault cytology test, in women from the West Midlands region of the UK.

To achieve this it is necessary to find out more information about those women that are undergoing hysterectomy operations: Who are they? Why do they undergo surgery? Is this related to their cervical screening history? What happens to them when they are in hospital? What was the final diagnosis from their operation? For those who had a total hysterectomy: Were they subsequently followed up by means of vaginal vault cytology? Was this done according to national guidelines and are there differences between those who were screened appropriately and those who were screened inappropriately?

A novel data linkage study was undertaken to establish this information and is reported herein.

CHAPTER TWO: BACKGROUND

INTRODUCTION TO CHAPTER

This chapter considers briefly how the 'research question' developed then summarises the relevant literature, including: information about hysterectomy operations, cervical cancer, cervical cancer screening programmes nationally and internationally and also the role of vaginal vault cytology testing after total hysterectomy. Work undertaken by the author in preparation for this thesis is also included. The chapter then explains the chosen research question and justifies the methodology selected to answer it by reference to the literature and concludes with the stated aims and objectives of this project.

The origin of the research question

This research arose from an audit undertaken at Birmingham Women's Hospital (BWH) NHS Trust Cytopathology laboratory, in 2000 (reported in a MSc thesis).[27] The audit considered the results of all vaginal vault cytology tests (vault smears) analysed there. Over the five-year period, February 1995 – January 2000, 5,080 vault cytology tests were processed: of these, 2,278 (44.80%) were generated in Primary Care, (Table 1), only one (0.02%) revealed any serious abnormality indicative of malignancy, forty four (0.87%) showed minor abnormalities or borderline changes, five (0.10%) contained endometrial cells, which implied that the hysterectomy had not been complete and 112 (2.20%) were deemed to be unsatisfactory for interpretation.[27]

These vault cytology tests represented over 2% of the workload of the Cytopathology department during this period (n=50,000 tests per annum, 250,000 in five years).

Table 1. Origin of vault cytology tests 1995 – 2000[27]

Source of vault tests	Total number of tests	% of total
Out-patient clinics	2,623	51.70
Primary care	**2,278**	**44.80**
Private hospitals / clinics	71	1.40
Family planning clinics	54	1.10
Hospital in-patients	28	0.55
Genitourinary clinics	26	0.51
TOTAL	**5,080**	**100.00**

These results led staff at the Cytopathology department to question why so many tests were being performed and if this was an appropriate use of resources. The vault cytology tests, particularly those from Primary Care, had poor detection rates, and thus the suspicion was raised that some tests were being undertaken inappropriately and not within the framework of national guidelines.

This led to a programme of work including: a questionnaire survey of healthcare professionals who undertake vault cytology testing, to establish their knowledge and behaviours, a systematic review of the relevant literature and a larger scale, audit of the records at BWH pathology department.[24;27;30] The conclusions suggested that there is a significant knowledge gap concerning vaginal vault cytology testing, in particular with respect to their use in primary care and the appropriateness of this.

2.1 HYSTERECTOMY

A clear distinction between, and understanding of, the various types of hysterectomy operation, and the risks and benefits of each, is essential if unambiguous messages are to be conveyed to primary care staff about requirements for ongoing cytological surveillance in women post-hysterectomy.

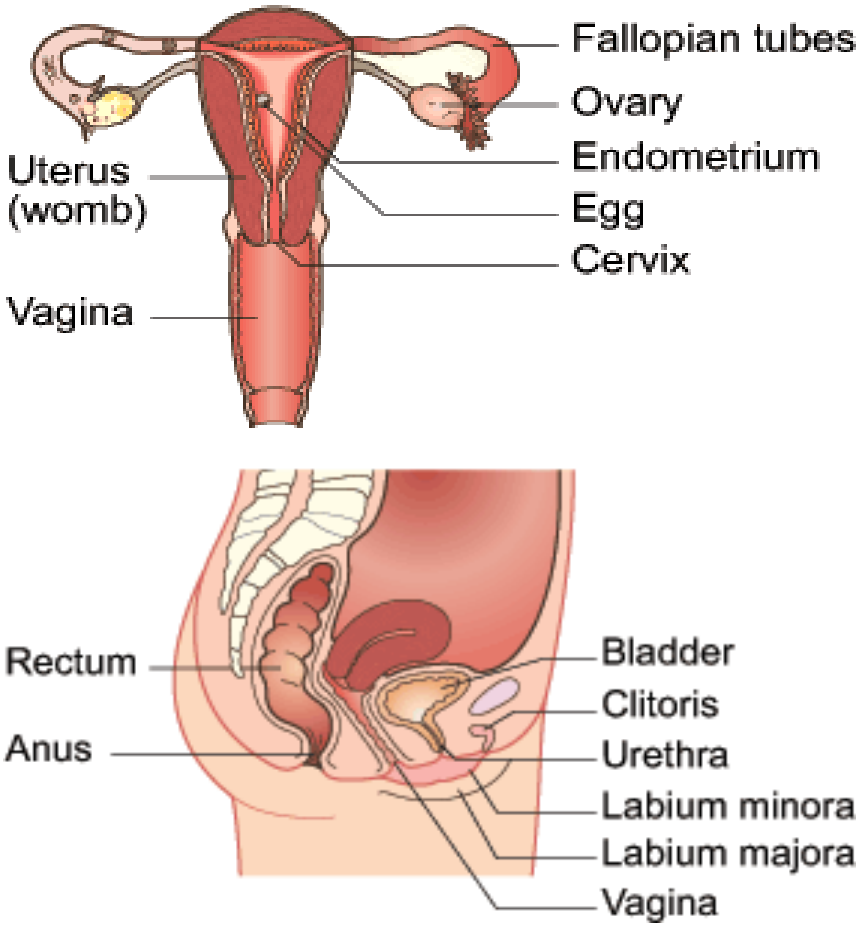
2.1.1 The hysterectomy operation and its variants

History of the hysterectomy operation

In the United Kingdom (UK) currently around 20% of the female population undergo surgical removal of the uterus during their lifetime[2,31,32] this operation is known as a 'hysterectomy' operation from Greek origin: *hysteros* = uterus or womb, *ectomy* = removal. Figure 2a & b illustrate the female pelvis and the organs that are usually removed during hysterectomy.

Geoffrey Chamberlain notes that hysterectomy had been performed before the advent of anaesthesia but was 'highly dangerous'; vaginal hysterectomy was noted to be somewhat safer and a successful vaginal hysterectomy was undertaken in Guy's Hospital, London in 1827.[33] Even with advances in anaesthesia it was only the introduction of the 'head down' operating position in the 1890's that pelvic surgery became safer and a realistic surgical option.

Figure 2a. & 2b. Female genital organs*



Total hysterectomy involves surgical removal of the uterus (womb) and cervix, leaving the vagina as a closed tube, deep in the female pelvis. Commonly the ovaries and fallopian tubes are removed at the same time. If the cervix is not removed this is called a 'sub-total' hysterectomy.

** Modified by the author, from NHS Direct, with permission*

Roy Porter comments that the subsequent surge in the numbers of hysterectomy operations in the 19th century was an "abuse of gynaecological surgery to control women" and that this was an operation performed by male surgeons who were all too keen to remove the uterus.[34]

In the twentieth century the 'total' hysterectomy became increasingly popular (see below) and overtook the 'sub-total' operation as gynaecologists realised that cancer could occur in the remaining cervical stump.[33] By the time of the First World War, abdominal hysterectomy was becoming the most commonly performed major gynaecological operation in the UK. However, as surgery frequently took place in the patients' own home, the outcome was highly variable.[33]

As antibiotics were introduced into routine surgical practice after the Second World War, hospitals became the natural home of surgery and as anaesthetic techniques improved so did the outcome of all types of major surgery.[33] From the 1960s onwards hysterectomy became routine surgery in most hospitals.[35]

Subtotal or Total hysterectomy?

Over 98% women who have their uterus surgically removed, in the UK, also have the cervix uteri or 'neck' of the uterus removed at the same time (called a 'total' hysterectomy).[4] This leaves the vagina as a pouch with a blind end at the site of amputation of the cervix (Figure 2a & 2b), this pouch is called the 'vaginal vault'. A partial or sub-total hysterectomy leaves the cervix in position and just removes the main body of the uterus. A radical hysterectomy involves removal of the vagina and the surrounding pelvic tissues and is usually reserved for the surgical management of malignancy. Any type of hysterectomy is frequently accompanied by removal of the Fallopian tubes and the ovaries; known as a 'bilateral salpingooophrectomy', commonly abbreviated to BSO.[4]

Subtotal hysterectomy has seen something of a recurrence in popularity, particularly in the USA, since the late 1990s, this has coincided with an expansion of laparoscopic technologies,[36] as the most risky part of laparoscopic hysterectomy is excision of the cervix and control of subsequent vaginal bleeding.[36] However, laparoscopic hysterectomy is still only a practised routinely by a small number of surgeons and does not account for all of the increase.[36]

In Denmark a large study (The Danish National Patient Register 2001) looked at hysterectomy over an 11-year period and noted that the number of abdominal hysterectomies had declined by 38% but the number of subtotal procedures had increased by a factor of 4.5x[37] this trend has not been reported in the literature in the UK.

A suggested reason for undertaking a subtotal procedure is that the cervical remnant may assist with supporting the pelvic floor, however, a large randomised controlled trial does not support this.[38] There are several known disadvantages of leaving a cervical remnant, including risk of persistent vaginal bleeding, cervical mucus discharge, cervical prolapse and the enduring risk of cervical neoplasia leading to a requirement for continued cytological surveillance.[36] Conversely, there have been claims than sexual satisfaction could be enhanced by cervical preservation, however, these have not been supported by any objective, high quality, evidence.[36] Subtotal abdominal hysterectomy may be quicker and easier to perform than a total hysterectomy, but these are probably the only genuine benefits.[39]

Since the 1980s many new treatments have evolved which have reduced the reliance on hysterectomy to treat various benign gynaecological disorders. These include assorted methods of destroying the lining of the uterus – the endometrium (ablative techniques), and innovative methods to obliterate the blood supply to benign tumours (embolisation techniques). However, hysterectomy remains the preferred procedure for removing pelvic tissue as it permanently and irreversibly removes the potential for future malignant gynaecological disease.[33]

Abdominal or vaginal hysterectomy?

A hysterectomy operation may be undertaken through the traditional surgical route of a vertical abdominal incision; however a 'Pfannenstiel' incision, made horizontally across the lower abdomen, is the route of choice for most gynaecologists, both approaches are termed 'abdominal hysterectomy'. Increasing in popularity, particularly in the last decade are less invasive approaches including vaginal surgery and laparoscopic (keyhole) techniques.[4] Vaginal surgery offers the prospect of faster return to normal activity, shorter duration of hospital stay and reduced risk of post-operative infections, whereas abdominal surgery allows greater access to the pelvis for the removal of large tumours and for extensive surgery (as in the case of malignant disease).[32] Laparoscopic hysterectomy requires greater surgical expertise and takes longer than the other methods but offers the shortest recovery times.[32]

Incidence of hysterectomy

Incidence and prevalence of hysterectomy has varied widely over the years and over geographic location: during the mid 1970s up to 50% of women in California had undergone the operation (prevalence) whereas at that time in Scotland it was 20%.[4] Hysterectomy has been declining in popularity in more recent years: estimates from the 1980s suggest that 100,000 women underwent the procedure annually; in England in 2002 - 2003 there were some 42,500 operations, whereas in 2007-08 there were 38,300 (Table 2). However, it is still one of the most commonly performed major operations as it is the definitive procedure for cure of many conditions.

In the USA around half a million women still undergo the procedure annually[36] but there remains significant variation between countries. Table 2 summarises the available international data.

Thus, at least a million women currently alive in the UK have had a hysterectomy procedure undertaken. With an ageing population this number will continue to rise, even though operation rates have been decreasing. As such it is important to establish if women need any form of ongoing cytological surveillance post-hysterectomy and, if so, on whom should it be undertaken.

Table 2. Incidence of hysterectomy worldwide[40]

Country	Number p.a.	Rate	Year of latest data	Source & Notes
England	38,328	13 per 10,000	2007-08	HES via DOH website. The Information Centre, England only, 2007-08[5]
England	74,000	26 per 10,000	1994-95	Dept of Health. HES England 1994-95 Vol 1 London HMSO 1996[41]
UK	100,000	35 per 10,000	1989	Vessey & Villard. Oxford Family Planning study, incidence of 20% by age 55yrs[2]
France	60,000	21 per 10,000	1997	Cosson. Retrospective case notes review[42]
Denmark	5,000	19 per 10,000	1998	Moller[37] and Gimbel.[14] Danish national patient register, sample of discharge summaries
Italy	-	37 per 10,000	1997	Materia E. Residents of Rome, hospital discharge records[43]
Finland	8,663	64 per 10,000 women aged over 35 years	1988	Luoto.[44] Finish hospital discharge register and 1987 population census, significant socio-economic variation
Norway	-	12 per 10,000 women	1982	McPherson.[45] National government data
Australia	30,000	45 per 10,000	2001-02	Australian council for safety and quality in healthcare, from national hospital morbidity data[46]
USA	550,000	56 per 10,000 women	1997	Farquhar C. National discharge data sample of 20% of US hospitals 1990-1997[3]. Life prevalence 33%, up to 43% in Utah[47]

Socioeconomic factors in hysterectomy incidence

It has been observed in the UK[1;2] and internationally[13;14;48;49] that, during the 1980s and 1990s, hysterectomy was more commonly undertaken in women of 'lower socioeconomic class' or women who were more 'deprived', the reasons for this generated debate in the 1980's and included (amongst others), associations with pre-cancerous cervical change and increased promiscuity in those of lower social class leading to more hysterectomy operations[1;50].

However, some exceptions to this pattern have been observed, particularly in Finland and in Los Angeles USA where more affluent women have undergone the operation more frequently, particularly for benign disease, this phenomenon seems to be associated with the higher availability of private gynaecology services to women of higher social class.[44;50;51]

Summary

Although the hysterectomy operation has attracted controversy because of its rise and fall in popularity,[52] it remains a very common procedure in the Western world. Consequently, all primary healthcare professionals will have patients who have already had, or will in future undergo, hysterectomy. Subtotal hysterectomy leaves part, or all, of the cervix in place whereas a total hysterectomy includes full removal. This has implications for any post-hysterectomy cytological surveillance.

2.1.2 Indications for hysterectomy, past and present

Over 90% of hysterectomy procedures are performed to cure benign conditions, despite the rise in very effective alternative treatment options, the majority undertaken for conditions which generate excessive menstrual blood loss, (see Table 4).[53] Excessive menstruation or 'menorrhagia' may be a major problem and some women become clinically anaemic and have their normal activities curtailed by it. Menorrhagia is the commonest cause of iron deficiency anaemia in the western world.[4]

In many women, no underlying disease process is detected and the term 'dysfunctional uterine bleeding' (DUB) is used to describe the phenomenon of menstrual blood loss of a volume deemed unacceptable by patients, although various other definitions exist.

Other causes of excessive menstrual blood loss include defects in the process of blood clotting i.e. Von Willebrand's disease, pelvic infections, the presence of a foreign body in the uterus i.e. a copper containing intrauterine contraceptive device (IUCD) or adenomyosis (a condition where endometrial tissue is detected deep in the musculature of the uterus).[54]

Other benign indications for hysterectomy include the presence of fibroid disease (smooth muscle, non malignant tumours) and endometrial polyps, both of which may present with excessive menstruation or because of pressure effects on other organs, or prolapse of the uterus and/or surrounding structures.

Pre-malignant disease makes a contribution to the incidence of hysterectomy: since the advent of routine cervical screening (see section 2.2) pre-invasive disease of the cervix is detected and treated in a variety of ways, depending on severity. To treat more serious or recurrent disease definitively a total hysterectomy, with excision of some vaginal tissue can be performed.

Malignancy of the vulva, vagina, cervix, uterus or adnexal structures (fallopian tubes, ovaries or ligaments) are all indications for hysterectomy; often more radical variants of the operation are performed to ensure a clear margin of tissue, free from any invasive disease, and thus minimise the opportunity for metastatic spread subsequent to surgery.[8]

Table 3 summarises the latest information concerning the incidence and mortality of the various types of gynaecological malignancy in the UK and latest estimates for the United States of America. It may be seen that cancer of the uterus (including endometrial and cancer of the body of the uterus) is the most common malignancy, closely followed by ovarian cancer, with vaginal cancer being very rare (six cases per million women).

Routinely collected statistics can be used to provide annual data incidence of hysterectomy in the UK, however, it is only by looking for emerging trends over time that we can understand what is actually happening to patients over their life course.

Table 3. Incidence of gynaecological malignancy[55;56]

Site of malignancy	UK incidence 2005 (actual) per 100,000*	UK mortality 2006 (actual) per 100,000*	USA incidence (estimated) per 100,000*	USA mortality (estimated) per 100,000*
Uterus	17.9	3.5	13.75	1.37
Ovary	17.4	10.1	7.0	4.72
Cervix	8.4	2.4	8.2	2.5
Vulva	2.3	0.6	1.2	0.3
Vagina	0.6	0.2	0.7	0.3

*incidences per 100,000 women (not head of population).

The last major survey of hysterectomy in the UK was published in 2002: the 'VALUE' study objectives were to describe hysterectomies performed in 1994 and 1995, their patients, surgery and short term outcomes.[1] The study collated data from about 45% of the operations during that year (n= 37,298) by self report from gynaecologists through England, Wales and Northern Ireland. Table 4 summarises these data and includes comparative data from an American study of a sample of national hospital discharge data covering 1990-1997.[3]

Table 4. Indications for hysterectomy (excluding malignancy)[1,3;57]

Indication*	**UK % of all**	**USA %**	**Notes**
Dysfunctional uterine bleeding (DUB)	43.46	13.46	Difference reflects variation in coding between these two diagnoses
Fibroids	17.74	40.53	
Prolapse	18.96	18.13	Very similar rates
Endometriosis / Adenomyosis	6.71	14.33	USA only stated endometriosis so some of their cases will be in DUB
Pelvic mass (excluding malignancy)	4.06	13.60	USA data did not have a pelvic mass category
Other	8.00		

Both authors noted that the large number of hysterectomies for fibroid disease and abnormal bleeding in the absence of malignancy were areas where operative incidence may be reduced in future, with the advent of endometrial ablative techniques and the licensing of a novel progesterone releasing intra-uterine system (Mirena® IUS) providing less destructive alternatives than major surgery.[1;3]

2.1.3 Outcomes and risks of surgery

Hysterectomy rarely leads to peri-operative death in the UK with a quoted incidence of just 1 in 4,000 operations,[9] however, major post operative and long term complications are more frequent. Table 5 summarises the most recent literature concerning complications of hysterectomy with approximate frequencies; estimates suggest that severe operative complications occur in 4.4% of hysterectomies.[1;57] Likelihood of complications increases with advancing age and presence of any co-morbidities.

Iversen and colleagues[58] used the RCGP oral contraception cohort study, of 23,000 women with over 20 years of follow-up on average, to establish that in the medium to long term hysterectomy was not associated with an increased risk of all cause mortality or with death from cardiovascular or malignant disease when compared to women who did not have a hysterectomy.[58]

It is a key aspect of high quality, contemporary, clinical practice that patients undergoing major surgery are provided with unambiguous information about the indication for surgery and the potential risks and benefits from it. In addition, patients should be offered a full discussion, with their surgeon, about all other available treatment options: hysterectomy inevitably has some significant risks associated with it, although it is usually regarded as 'routine surgery' and the risks to any one individual are low.[9]

Complications that matter to most patients include changes in their quality of life, sexual function, pelvic pain, bowel and urinary function and vaginal prolapse.[32] Overall quality of life for women who have been suffering from prolonged abnormal uterine bleeding (the commonest indication for hysterectomy) has been shown to be significantly improved at six months and two years after surgery.[59] Thus although it is a major procedure with the potential for serious complications, most women who undergo a hysterectomy are happy with the outcome and gynaecologists regard it as highly effective, this may go some way to explaining why, despite many viable alternatives, it remains such a popular operation.[39]

Table 5. Complications of hysterectomy operations

Operative complications	**Frequency**	**Notes or source of data**
Intra-operative death	0.025%	Nil reported in latest series[1;9]
Major haemorrhage	2.27%	Maresh, Value study[1]
Damage to pelvic organs / viscera	0.73%	
Respiratory / Cardiac complication	0.35%	
Need to return to theatre	0.76%	
All operative complications	*3.50%*	
Post operative complications		
Death (within six weeks)	0.04%	Maresh, Value study[1]
Severe cases (includes death, thrombosis, myocardial infarction, renal failure, stroke, septicaemia, necrotising fascitis, secondary haemorrhage, fistula, ureteric obstruction, visceral damage and late return to theatre)	1.03%	
Not severe cases (wound problems, all infections, pelvis or urinary tract related, incontinence, adhesions, bowel obstruction, anaemia, anaesthetic problems, pyrexia, nerve entrapment, depression, psychiatric symptoms or sleeping difficulties.)	7.67%	
All	*8.59%*	
Long term complications[57;60]		
Altered sexual function	Nil	Farrell[61] old studies had negative findings but high quality research consistently reports improvement
Altered bowel function (including constipation)	5.0%	Thakar[62] Most studies retrospective, no conclusive evidence of causation
Altered urinary tract function	Up to 20%	Vierhout[63] Most studies retrospective, and again no conclusive evidence of causation
Vaginal vault prolapse	0.2 – 1.0%	Barrington[64]
All pelvic prolapse	5%	Blandon[65]
Quality of life	Improved for most	Kupperman[59]

2.2 CERVICAL CANCER AND THE NATIONAL SCREENING PROGRAMME

Follow up after hysterectomy using the vaginal vault cytology test uses the same techniques, technology and NHS systems as those already established to screen for cervical cancer. This section will thus outline the aetiology and natural history of cervical cancer and the justification and implementation of national and international screening programmes as this has implications for the delivery of vaginal vault cytological testing.

2.2.1 The natural history of cervical cancer

Cervical cancer (carcinoma of the cervix) has been known since ancient Egyptian times, when it was treated by cautery.[33] It is currently the third commonest cancer in women worldwide, after breast and bowel.[66;67] In the UK currently it is the 11th commonest cancer of women; this significant difference is due primarily to the highly successful national screening programme used to detect pre-invasive squamous disease of the cervix and treat it before it develops into malignancy.[15;68] Cervical cancer deaths worldwide occur mainly in the developing world (80%) where, in many regions, it is the commonest cancer affecting women.[66]

Cervical cancer can take several forms; squamous cell type is the commonest (at least 90%) which tend to occur in the squamo-columnar junction of the cervix, then adenocarcinomas or tumours 'of glandular origin' comprising the rest, (less than 10%), tending to occur within the cervical canal.[8]

Where no effective screening programmes exist, the incidence of cervical cancer rates have remained relatively constant over time: incidence rises rapidly in the age group 25-40 years then reaches a plateau and eventually decreases a little in women over the age of 70 years.[66] However, where changes occur in sexual behaviour of populations (increasing numbers of sexual partners) a rise in incidence occurs in younger age groups.[66]

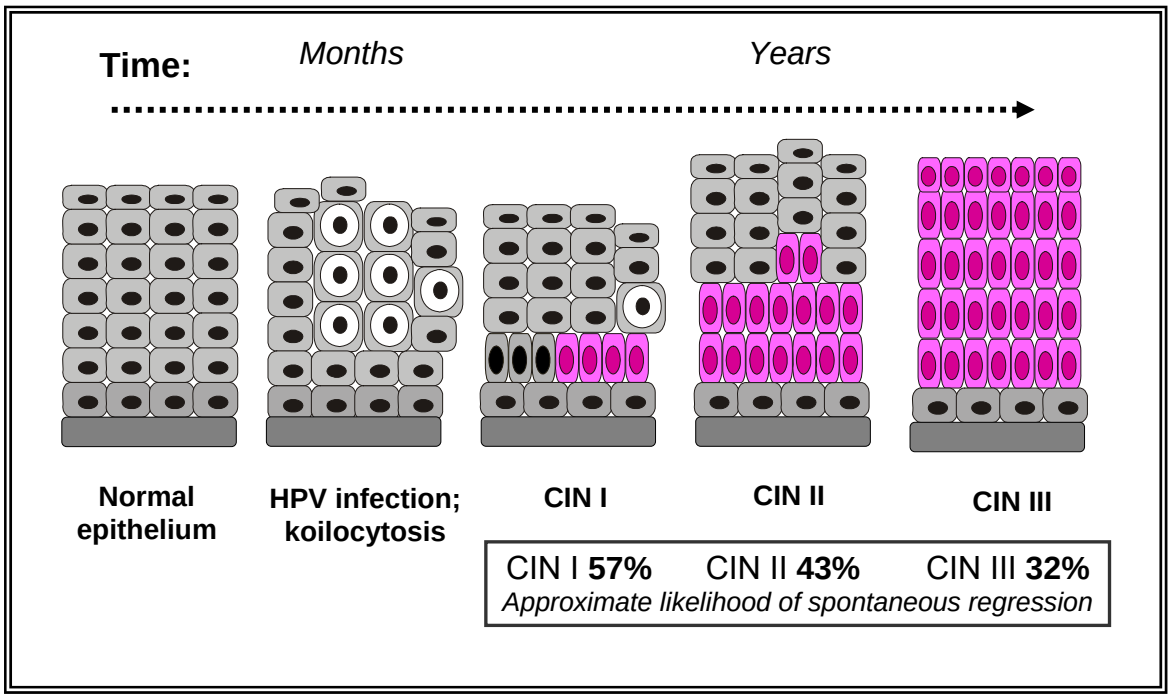
Squamous cervical cancer has a well established 'natural history' whereby early changes in cervical tissue may progress to invasive disease. This pre-cancerous stage is known as Cervical Intraepithelial Neoplasia (CIN) and is categorised in three main stages (CINI, CINII and CINIII), illustrated in Figure 3. It is possible for any of these stages to regress but the more advanced the disease, the less likely that this spontaneous regression will occur. Currently it is estimated that, if left untreated, approximately 90% of changes induced by infection with human Papilloma virus (HPV) will regress spontaneously within 12-36 months as the human immune system eliminates the virus, see Figure 3 and section 2.2.2 for explanation of the role of HPV.[69]

Although estimates vary widely, up to 80% of CIN I will probably regress spontaneously if left untreated[66;70] whereas approximately 30% of CIN III will. Having any such abnormality significantly increases the risk of developing cervical cancer over background rates.

Rate of natural progression through these stages usually takes several years. A study by McIndoe and colleagues (which could never be repeated for ethical reasons), considered 131 women who had been diagnosed with CINIII and he followed them up, without treatment, for several years; after 20 years 36% had developed invasive disease. [71]

Nomenclature concerning CIN and dyskaryosis is confusing to those who do not use it regularly, Table 6 includes three different histological schemes; the Bethesda scheme,[72] introduced to simply the classification, is not widely supported in the UK, where 'scheme 2' is in use. The term carcinoma in situ is no longer in favour but is found in much of the literature in this area and the reader needs to understand where it sits in the order of disease progression.

Figure 3. Progression of cervical cellular changes in CIN*



* *Adapted, by the author, from GSK 'notes for speakers', with permission*

An exfoliative test to detect cellular changes that may be indicative of CIN was developed by George Papanicolaou (1883 - 1962). In 1941 he published a definitive paper about his work on identification of cervical cancer in cells scraped from the walls of the vagina and cervix.[73] In 1947 a spatula (Ayre's) was produced to obtain an optimum exfoliative sample of cells and the cervical 'smear test' or 'Pap' test was gradually adopted.[35]

The nomenclature used for describing abnormalities detected by these screening tests has varied over time and there have been problems with intra-observer variation in classification. The correlation between results obtained by means of screening tests and the histological results obtained from biopsy is variable.[70] The term dyskaryosis is applied to abnormal screening tests but mild dyskaryosis does not translate perfectly to mild dysplasia or CIN I, although they are associated. Thus direct comparison of cytological test results and histological description of biopsy specimens is not technically accurate.[72]

Table 6. Terminology for describing squamous cell lesions*

Scheme 1	Scheme 2	Bethesda
-	HPV changes	Low grade lesions
Mild dysplasia	CIN I	
Moderate dysplasia	CIN II	High grade lesions
Severe dysplasia	CIN III	
Carcinoma in situ		

* *NB. These terms, across the three schemes, are not interchangeable but are aligned to allow for meaningful comparisons*

2.2.2 Risk factors for developing CIN

There are several factors associated with a risk of developing the pre-invasive stages of cervical cancer. The first, and most critical of these, is undoubtedly the presence of infection with an oncogenic strain of the Human Papilloma Virus (HPV) at some time.[66;69] Believed to be an essential step in disease progression, this family of small DNA viruses has over a hundred known sub-types, of which, forty have been associated with cervical and other lower genital tract cancers (vulval, vaginal and anal in women and penile and anal cancers in men). Transmitted via skin to skin or sexual contact[69] they are highly prevalent[74] and it is estimated that up to 70% of women have been infected at some time.[75] Most infection is asymptomatic and routine testing for HPV is not currently available in the UK.[74;76]

Recently two highly effective vaccines have been launched to protect people against two oncogenic subtypes of HPV (16 & 18) which are responsible for triggering over 70% of cervical cancers.[69] National immunisation programmes are now underway in many Western countries to ensure that all girls under the age of 18 are immunised.[77;78] It is envisaged that this intervention has great potential to reduce deaths from cervical cancer, although it will take many years for this to be realised due to the slowly progressing nature of the disease and that these girls are currently very young.[77] There is a strong argument for women who are HPV naive but are older than 18yrs of age, being vaccinated, however cost-effectiveness concerns have tended to age-limit public programmes.[79]

Other factors that increase the likelihood of developing pre-malignant disease of the cervix include: greater social deprivation, poor uptake of cervical screening opportunities, presence of HIV infection, smoking, long term use of oral contraceptives, higher parity and higher numbers of pregnancies, early age of first intercourse and multiple sexual partners.[80] Cervical cancer survival is strongly related to screening history as 'screen detected' disease is usually found at an earlier stage than disease that presents symptomatically. Survival is also related to access to optimal cancer care and, until 2000, this was uneven throughout the UK.[67;81]

2.2.3 The NHS Cervical Screening Programme (NHSCSP)

Cervical screening in the UK, using the Papanicolaou smear test, began to be adopted by doctors in the 1960s and by the mid-1980s many women were having regular tests done opportunistically by their General Practitioner, but there was concern that those at greatest risk of cervical cancer were not being tested.[82] In addition, it was suspected that those with positive screening results were not being followed-up and treated effectively or consistently across the country.[82] Consequently, the NHS Cervical Screening Programme (NHSCSP) was established in 1988, when the Department of Health instructed all health authorities to introduce computerised call/recall systems and to meet certain quality standards.[82]

There is a large body of scientific evidence which states that both the incidence and mortality from squamous cancer of the cervix can be reduced by well-organised screening programmes.[66] Indeed, in the UK alone, it is now estimated that 5,000 lives are saved annually by the cervical screening programme[15] (4,500 in England) and that the programme is directly responsible for the 42% drop in the annual incidence of cervical cancer observed between 1988 and 1997.

The single most important factor in this improvement is the significant increase in screening coverage: in 1988/89 only 44% of the target population of women aged 25-64 were screened every five years, in the late 1990's 85% of the same target population were being screened. However, since 2000, this proportion has been falling, and although coverage in women over 50 years has been sustained at over 80%, in younger women five-yearly screening levels are below 79% and the three and a half yearly target for women under 50 years is achieved in less than 70%.[15]

The stated aim of the NHSCSP is to reduce deaths from cervical cancer.[83] It is funded by regional health authorities, from their overall budgets.[82] The national cost is estimated at approximately £132 million per annum, or £34 per woman screened.[82] The actual number of women screened in 2007/08 was 3,223,239, an increase of over 50,000 on the previous year. The number of tests that were inadequate for interpretation fell by around 50,000, thus there has been a considerable improvement in efficiency and coverage.[15]

The proportion of tests that are taken in Primary Care has slowly been increasing, in 2003 it was 92.1% but in 2007/08 it was 93.8%. Overall the total number of tests taken has fallen (as inadequate rates fall, fewer women needed to have repeat tests), but the decrease appears greater from secondary care.[15]

Women who have abnormalities detected are either referred to a local colposcopy service for further investigation or a repeat test is advised. Table 7 summarises the various test results and recommended actions, these are nationally set. Of those referred to colposcopy: 17% are because of persistently borderline changes, 31% for mild dyskaryosis, 14% moderate and 14% severe disease. Less than 1% are referred for potential invasive cancer and 1% for potential glandular cancer.[15]

Table 7. Management of abnormal cervical cytology results[84]

Screening test result	Histology	Action recommended
Normal	0.1% CIN II-III	Repeat 3 / 5yrs depending on age
Inflammatory	6.0% CIN II-III	Repeat 6m
Borderline nuclear changes	20-37% CIN II-III	Repeat 6m
Mild dyskaryosis	50% CIN II-III	Refer colposcopy
Moderate dyskaryosis	50-75% CIN II-III	Refer colposcopy
Severe dyskaryosis	80-90% CIN II-III	Refer colposcopy
Severe dyskaryosis 'positive' or 'malignant cells'	5% invasive disease	Refer colposcopy
Invasion suspected	50% Invasion	Refer colposcopy - Urgent
Abnormal glandular cells	Possible adenocarcinoma of the cervix or endometrium	Refer colposcopy - Urgent

Since 2005, further to successful regional trials, a novel approach to the processing of cytological samples from the cervix was introduced throughout the UK: Liquid Based Cytology (LBC) has been implemented nationally since 2007 and has already led to a reduction in the number of inadequate samples generated.[85]

LBC represents a combination of a new sampling device (a soft brush that is rotated over the transformation zone), a new transport medium (a suspension into which either the entire brush head or the cells from the brush are deposited) and an automated system for the processing of samples.[85] All primary healthcare professionals who routinely take cervical cytology had to be re-trained to learn this new technique; however, training did not include sampling of the vaginal vault. The soft brush sampling device does not lend itself to this variant of the test as well as the Aylesbury spatula used to.

With the reduction in numbers of tests being processed, Cytopathology laboratories have been actively trying to reduce the time taken to process samples and generate the result; over the past five years this has improved with 49% of results being available within a fortnight and 83% within four weeks, compared with only 70% in 2003/04.[15]

In England and Wales the age-standardised incidence of cervical cancer in the 1970s and 1980s remained between 14 and 16 per 100,000 (excluding some specific cohort effects);[67] in 2000 it was below nine per 100,000.

Although overall coverage of the screening programme is very good there has been a noticeable decline in the proportion of younger women attending for screening. There is concern that if coverage of screening falls further then there will be a concomitant rise in cervical cancer in the future and significant efforts are being made, both nationally and locally, to recruit younger women back to screening programmes.[15;86]

Since the death of a young, UK celebrity in 2008, from cervical cancer, and the introduction of the national HPV vaccination programme in the same year, there has been considerable media attention on the subject of cervical cancer. The 'Jade Goody effect' appears to have had a substantial impact on increasing uptake of screening in women aged 25-30 years, however formal data is awaited.[87]

In any screening programme resources may be used inappropriately. Vaginal vault cytology tests should not normally be paid for under the auspices of the national cervical screening programme. By definition, they are not a screening test for pre-invasive disease of the cervix, as no cervical tissue remains. A cytology test taken from cervical remnants after less radical surgery should not be called a 'vault smear' or 'vault cytology' as this could cause confusion in the interpretation of the slide; it is still a cervical cytology test.

2.2.4 Screening for cervical cancer: The international perspective

The World Health Organisation recommends that any screening test should only be adopted and implemented if it fulfils several criteria. These criteria, identified and publicised by Wilson and Junger,[88] suggest that 'screening' is a process of identifying individuals who are at sufficiently high risk of a specific condition to justify further investigation or treatment.

Screening tests are systematically offered to a population who have not sought medical attention or do not display symptoms of the condition which is being tested. The aim of screening programmes are to benefit the individuals being tested: thus there is an ethical imperative to ensure that any screening tests are sensitive, specific, cost effective and acceptable to patients and to minimize the potential for harm. It is also important that patients realise that screening tests are fallible and that false negatives will occur.

We know the natural history of cervical cancer; there is often a long time between first detectable cellular changes and progression to serious disease, particularly with respect to squamous cell carcinoma. Inevitably many women will be identified as being at risk of disease when in reality only a small number would ever go on to develop cervical cancer, thus many women will be unnecessarily worried and further investigated due to an abnormal test result.

To minimise this harm a balance must be struck between over testing, and thus inevitably having more false positive results, and screening too infrequently and missing genuine cases.

To run a successful cervical screening programme issues to be tackled include: funding and resources, training of healthcare practitioners, provision of quality assured laboratories, referral and treatment pathways, national monitoring systems for 'call and recall' and education of the population to ensure participation.[66]

Worldwide there are significant variations in approaches to screening for cervical cancer: In most affluent nations screening exists but there is wide variation in how this is undertaken, by whom and how often.[66] Deaths from cervical cancer in developed countries occur mostly in women who have never been screened and the greatest mortality is in women aged over 50. The reader is directed to the International Agency for Research on Cancer (IARC), of the World Health Organisation (WHO), handbook on cancer prevention series, volume 10 which collates world wide data on this subject of cervical cancer.[66]

The European Union recommended cervical screening in all member states, in 1987, and issued quality assurance guidelines in 1993. However, coverage is still variable ranging from comprehensive programmes with good coverage in Denmark, Finland, Norway and Spain through to pilot programmes in Eire, Greece and France.[66]

Age of screening is also variable with Luxembourg starting screening sexually active girls of 15 years but Finland, Sweden and Netherlands starting at 30 years. Cessation of screening occurs between 59 and 69 years.[66] Screening is undertaken in both primary and secondary care and five-year coverage (i.e. the proportion of the eligible population having at least one screening test within five years) ranges from 40% in Spain to over 90% of women in Finland.[66]

In the USA provision of cervical screening is variable and depends upon personal circumstances with the well-insured being offered annual screening as part of routine health checks but the uninsured dependent on State programmes which vary widely; many women are not eligible. In Canada there is universal coverage of cervical cancer screening which is devolved to provinces to administer; most screening has been opportunistic although this is changing as organised programmes with call and recall are introduced. In Australia cytological testing has been available from the 1960s with a national screening programme being introduced in 1995 on a two-year screening interval (18 – 69 years). In Africa screening is difficult to achieve because of competing healthcare needs of the population and a lack of resources, additionally, the higher prevalence of HIV infection is a profound problem, which in turn impacts upon the incidence of cervical cancer.[66]

Universal availability of screening for cervical cancer is an international health aim, as there are profound variations in practice.

2.3 VAGINAL VAULT CYTOLOGY TESTS (VAULT SMEARS)

Screening after total hysterectomy by examining a cytological sample taken from the scarred region of the vagina where the cervix used to be located (the vault), is used variably by clinicians. This section defines the anatomy, explains the national guidelines and testing process and explores the current evidence for use of the test in clinical practice.

2.3.1 What is a vaginal vault cytology test (vault smear)?

Total hysterectomy includes removal of the cervix-uteri (called the cervix hereafter), and leaves the vagina as a blind ending pouch; this pouch is known as the vaginal vault. Since the cervix has been removed completely there is no possibility of the development of a primary cervical cancer and thus no indication for routine cervical screening. Papanicolaou (Pap) tests of the vaginal vault are a means of detecting recurrent invasive or pre-invasive disease of the lower female genital tract (Vaginal Intra-epithelial Neoplasia – VaIN) in women who no longer have a cervix.[31] Subtotal hysterectomy is an indication for continued participation in the routine cervical screening programme, however, as explained in Section 2.1.1, subtotal surgery is undertaken in less than 3% of the hysterectomies performed in the UK.[1]

2.3.2 Indications for undertaking vault cytology tests

2.3.2.1 National guidelines[89,16,83]

Screening using vaginal vault cytology tests fall outside the NHSCSP (see section 2.2.3 for details of NHSCSP), as they are not used to prevent cervical cancer. However, there are some guidelines relating to appropriate use, these are listed in Figure 4 and apply to both primary and secondary care clinicians.

Figure 4. Summary of NHSCSP guidance: use of vaginal vault cytology[16]

- For women on routine recall for at least ten year prior to hysterectomy and no CIN in the sample at hysterectomy, no vault cytology is required.

- For women with less than ten years routine recall and no CIN at hysterectomy, a sample should be taken from the vault six months after surgery and there should be no further cytology follow-up if it is negative.

- For women with completely excised CIN at hysterectomy, a sample should be taken from the vault at six and eighteen months after surgery and there should be no further cytological follow-up if both are negative.

- For women with incomplete or uncertain excision of CIN, follow-up should be conducted as if the cervix were still in situ.

Thus, national guidelines suggest only a limited role for vaginal vault cytology tests. However, these guidelines are largely based on expert opinion and do not specify what further role vault cytology testing should have in the follow up of women following abnormal results or following a hysterectomy where malignancy was detected. This is currently left to the discretion of the treating clinician.

2.3.2.2 A systematic review of the literature: the use of vaginal vault cytology tests

In view of the lack of 'gold standard', prospective, randomised controlled trial evidence underpinning the national NHSCSP guidelines concerning vault cytology tests, a full systematic review of literature was undertaken by the author (as PI) and departmental colleagues, and reported in full in the British Journal of Obstetrics and Gynaecology in 2006.[24]

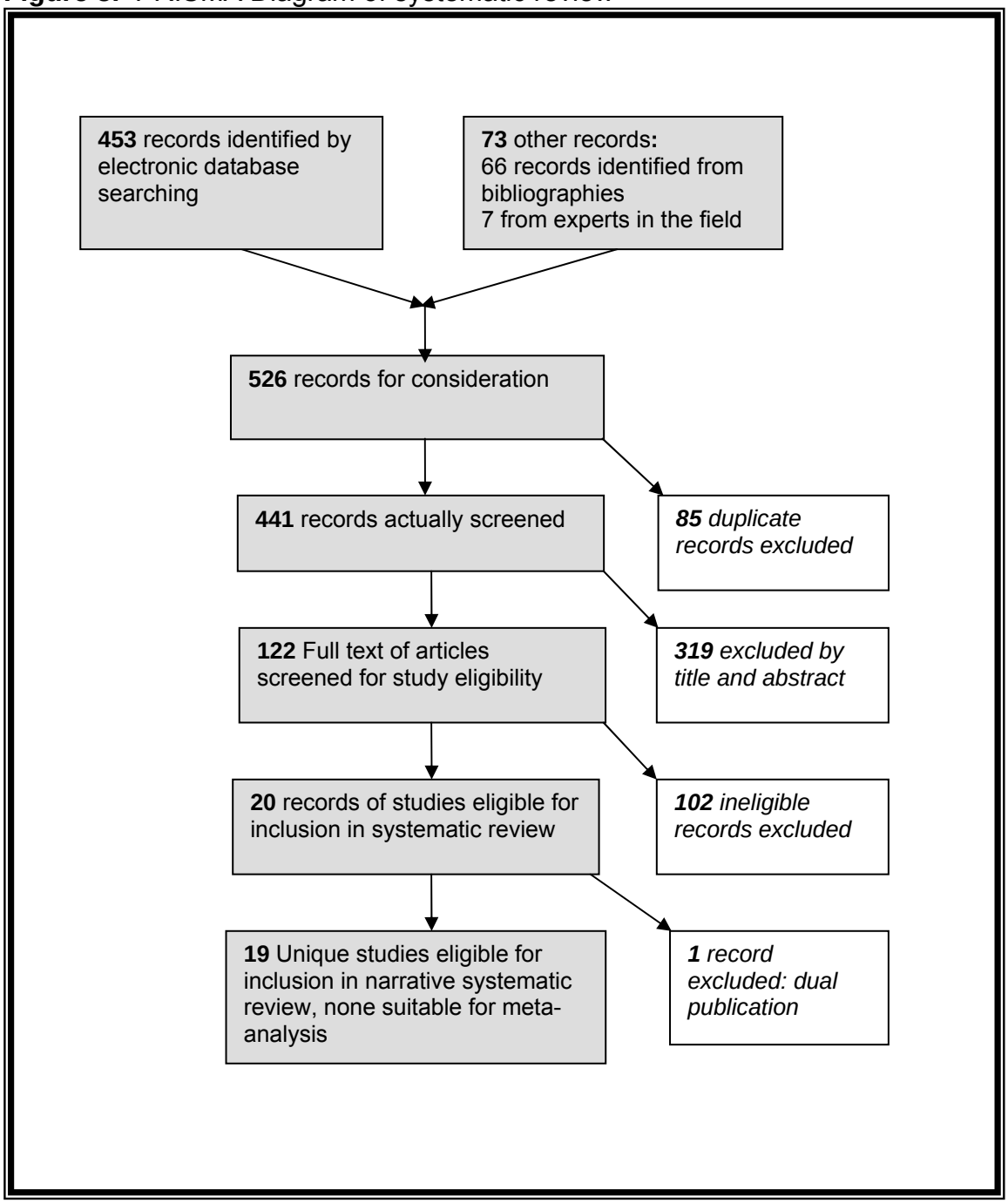
The aim of the review, performed to Cochrane standards, was to establish the evidence base for the use of vaginal vault cytology subsequent to hysterectomy for benign or pre-cancerous conditions. This was done by identifying all studies that reported the follow-up of a series of patients treated by hysterectomy for reasons other than malignancy, and contained data to enable the effectiveness of vault smears in identifying VaIN to be estimated. Papers were 'eligible' for inclusion if they reported on a population of women who had undergone a hysterectomy and at least some of the population had vault cytology tests. Case reports or expert opinion were excluded.

Results of the systematic review:

The review identified 526 citations but after eligibility and validity assessment only 19 remained.[20;22;23;43;71;90-98;98;98-103] All 19 utilised a form of cohort design, one included a control group.[103] The included papers were published between 1963 and 2000 in 16 different journals, with 11 published prior to 1990 (58%). There were no papers concentrating exclusively on women who had CIN I or CIN II, the majority of papers considered follow up after carcinoma-in-situ or CIN III.

Appendix A includes the full published paper including the main data table and Figure 5 is the PRISMA diagram of the review process.[104]

Figure 5. PRISMA Diagram of systematic review[104]



The better quality studies had a combined study population of 11,656 hysterectomies of which 6,543 were for benign disease, 76 for CIN I/II and 5,037 for CIN III. Nevertheless, incompleteness of follow up and recording of data prohibited any meta-analysis of the data and thus it was not possible to provide robust estimates of the value of the vaginal vault cytology test in the follow up of women who have had a hysterectomy for reasons other than malignancy.

There was little good quality evidence concerning the role of vaginal vault cytology tests and there were insufficient data to enable the calculation of robust aggregated assessments of the sensitivity or specificity of the test. Most of the observed events occurred within the first two years of follow-up; 46 of the 48 documented abnormal tests occurred within two years of hysterectomy. Of the six best quality studies, two considered data from women who had a hysterectomy for benign indications or CIN I/II and four studies considered women who had CIN III.

The aggregated data from studies following-up over 6,800 women after hysterectomy for benign indications, CIN I and CIN II showed that despite up to 50 years follow-up, no cases of subsequent vaginal cancer were identified. Only one case of vaginal cancer was observed, three years after hysterectomy, in the cohort of 3,569 women having hysterectomy for changes of CIN III. Unfortunately, all the studies following up women after hysterectomy with CIN III had significant methodological or reporting flaws.

Thus the conclusions were that primary vaginal cancer is very rare and does not warrant any screening programme and that the current UK guidelines (Figure 4) seem sensible.[24] The study also confirmed the need for definitive research to determine the appropriate duration and frequency of vaginal vault cytology tests after hysterectomy, for reasons other than cancer. As it is not practical to undertake a prospective randomised controlled trial (because vaginal cancer is rare and such a trial would have considerable ethical implications), epidemiological techniques offer the most practical approach to answering some of these questions.

There is currently no evidence to suggest that there is demonstrable benefit in screening after hysterectomy for benign disease[24;105] and there is no evidence to support changing current guidelines for screening after CIN I/II. Screening after CIN III for five years was proposed by some authors, however, the data indicated that 95% (46 of 48) of all abnormal tests occurred within two years of hysterectomy and only one case of vaginal cancer was identified in all of the reported series.

The value of the vaginal vault cytology test as a screening tool after hysterectomy for reasons other than existing cancer is not supported by the existing literature.

2.3.3 When are vault cytology tests being undertaken?

2.3.3.1 Questionnaire survey of primary healthcare professionals

This study aimed to establish primary care professionals' (GPs and Practice Nurses) knowledge and perceived behaviour relating to the use of vault cytology tests and has been fully reported in Cytopathology.[30]

Results of questionnaire survey

This postal questionnaire survey achieved a response rate of 68.6% (n=291) with practice nurses having a higher response rate than GPs (p=0.007). The frequency of performing vault cytology tests was assessed by self-report and nurses took significantly more tests than doctors (p<0.001). There was no significant difference in knowledge between doctors and nurses or between male and female respondents. However, a comparison of the 'knowledge score' against the reported frequency of performing vault cytology tests suggested an inverse relationship; those with higher scores (better knowledge) undertaking the test least often (Kruskall Wallis χ^2=10.87, df =5, p=0.054).

Conclusions of questionnaire survey

Vaginal vault cytology tests incur a cost both to the NHS and the patient. Those practitioners with higher knowledge scores tended to report performing fewer tests. If all primary care professionals had practised according to current guidelines the number of vault cytology tests undertaken would have been reduced.

The modification of professional behaviour is not simple, however, this study suggested that a simple educational intervention (a letter was sent from the laboratory to every registered sample taker) could result in a reduction in the numbers of vault cytology tests being performed; thus leading to savings in both resources and the emotional cost to patients.[30]

2.3.3.2 Audit of histopathology records at Birmingham Women's Hospital

This large audit work was undertaken as a pilot project for this thesis and is awaiting publication in Cytopathology; Appendix B includes the paper that was sent out to review.[28]

Background

The Pathology Department and Cytology Laboratory at the Birmingham Women's Hospital Health Care NHS Trust (BWH) has had comprehensive computerised records since 1995. These comprise the personal and contact details of patients, clinical details, and results of all their histological and cytological specimens. The study aimed to assess whether current national guidance on who should have a vault cytology test was being followed by: identifying women who had hysterectomy operations 1995 - 2005, describing their demographics, describing any subsequent vault cytology tests and determining whether or not these were in accordance with national guidelines.

An electronic search of the computerised records for the period 1st April 1995 to 31st March 2005, was run, looking for the topography (T) codes identifying hysterectomy samples. Patient identifiers were then used to identify and link any other relevant department records. The records were also searched to identify vault cytology tests by means of a laboratory based 'text' code.

Results

There were 8,457 records of separate vaginal vault cytology tests during the study period representing 3,164 different women. The number of vault cytology tests per woman ranged from one to 17, with 47% of women having just one test and over 87% having five or fewer during the ten-year study period (mean=3.06, median=2). Age at vault cytology followed a near normal distribution (range: 17 to 95 years, median=52 years). The median age of women having vault cytology tests increased over time (Pearson correlation=0.922, $p<0.001$).

General Practice was the most frequent setting for vault cytology tests, followed by gynaecology outpatient clinics. The origin of vault cytology tests varied over time with a greater decline in numbers from general practice, other community settings and outpatient clinics than from the colposcopy service: GP and community sources versus all other vault cytology tests, χ^2 for linear trend=4.8 (9df, p=0.028); ward, theatre and out patient tests versus all other settings, χ^2 (linear trend)=139.53 (9df, $p<0.0001$); colposcopy versus all other sources, χ^2 (linear trend)=87.33 (9df, $p<0.0001$).

There was a downward trend in total numbers of vault tests analysed each year. Abnormalities were detected in 8.9% of tests, with malignancy being detected in less than 0.1%. The 'unsatisfactory sample' rate of 10.7% compared favourably with the in-house 'unsatisfactory' rate of 11.6% during the study period.

Dyskaryosis was reported in just 4.4% of the samples, and invasion was suspected in less than 0.1%. The eight tests indicating malignancy were performed on four women, one of whom had fourteen vault tests taken during the ten-year study period, four of them indicating malignancy. The pattern of results suggests that not only were fewer tests being done, as the years passed, but that lower grade abnormalities were being detected.

General Practice and the community setting had particularly low detection rates for significant abnormality over the decade: no malignancies and only two severe abnormalities were detected from almost four thousand vault cytology tests taken in primary care. 'Abnormal' tests (borderline, mild, moderate, severe or malignancy) represented only 2.8% (113) of the total, with the majority (n=73) of these being 'borderline' results; whereas for the hospital settings (clinics, wards and operating theatres) the proportion of 'abnormal' test results was 14.5% (n=616).

All the cytology results that indicated cancers (n=8, from four women) were detected in tests taken in gynaecology or colposcopy clinics and all were in women aged over 60. Of the 93 samples, in 39 women, that demonstrated 'severe' abnormalities, only three were taken in the community setting.

Summary of audit

There was a steady fall in the number of vault cytology tests processed annually; this was particularly noticeable from primary care and gynaecology out-patient clinics. The average age of women having vault cytology tests appeared to be increasing over time and the most significant abnormalities were, nearly all, detected in secondary care settings.

The decline in the number of vault cytology tests during this period was far greater than the decline in the number of cervical cytology tests and could not be explained by national or local trends. Within the ten year study period, research undertaken by the authors (2001-2003) may have increased primary care practitioners awareness about inappropriate use of vault cytology tests,[30] and may have contributed to the decline in vault tests undertaken in the community.

There was a very low rate of cellular abnormalities detected by testing; the vast majority of results were normal or of no clinical significance: over 84% did not demonstrate any significant abnormality, 10.7% were unsatisfactory for interpretation. Of those that did demonstrate an abnormality (382=4.4%), most were either mild or moderate changes (n=281). Only 1.2% of all the tests (101 from 8,457 tests) from 1.4% of all the women (43 from 3,164 women) demonstrated a serious abnormality. These results suggest that vault cytology tests were not being restricted to higher risk women.

In this population, this test appears to have had poor detection rates for disease. In particular, tests being done in the community setting were highly unlikely to detect any significant abnormalities, thus calling into question the usefulness of the vault cytology test in the community.

Thus, it would appear that use of vaginal vault cytology tests has been declining, this appears appropriate given the poor detection rates for disease, particularly in asymptomatic women following hysterectomy for benign indications.

It was concluded that to establish the true value of vaginal vault cytology tests it would be necessary to access more comprehensive data about women's entire screening histories, their hysterectomy pathology results and the results of any subsequent vault cytology tests.[28] Then vault cytology tests could then be assessed for their appropriateness and conclusions drawn.

2.4 DEVELOPING AN APPROPRIATE STUDY DESIGN TO RESOLVE THE QUESTION OF: WHEN SHOULD VAGINAL VAULT CYTOLOGY TESTS BE USED?

2.4.1 Summary of the literature and justification of methodology

When the findings of the systematic review were published it was evident that there was a dearth of high-quality evidence concerning appropriate use of the vaginal vault cytology test in both primary and secondary care. The available literature was sparse and of poor quality for the purpose of determining when vaginal vault cytology should be used; national guidelines are thus based on inadequate evidence.

What has been established is that primary care clinicians (doctors and nurses) know little about the test and most clinicians appear to use them inappropriately,[30] taking twice as many as the guidelines recommend in those who start having tests but then not taking vault cytology tests at all in a significant proportion of women who, the guidelines suggest, should be screened.[30]

Guidelines are known to improve care and standardise behaviour between clinicians[106] however, changes in guidelines are difficult to implement and there are many examples of patients receiving inappropriate care in the presence of guidelines.[107;107;108]

Vaginal cancer is a rare malignancy and none of the evidence that has been collated suggests that vaginal vault cytology would make an appropriate national screening tool. Any study to investigate this matter further would require large numbers of women.

A population based or 'epidemiological' approach to look at women who undergo a hysterectomy was deemed to be the most appropriate next step in answering the research question *'when should vault cytology tests be performed post hysterectomy?*'

The basis of this research should be an observational cohort of women undergoing total hysterectomy, for any indication, reviewing their cervical cytology prior to surgery and then establishing if they subsequently undergo vaginal vault cytology following hysterectomy. This would provide valuable information as to current practice on a larger scale than that reviewed by the audit and would give more generalisable results. By describing an up-to-date cohort of women undergoing hysterectomy and their diagnoses at surgery, supplemented by information from their entire cervical screening histories, this research would provide a unique insight into this subject and provide the high quality evidence that is currently lacking. Chapter 3 explains the chosen study methodology in detail.

2.4.2 Population based data sets

Developments in technology have meant that there are now multiple databases available, providing secondary sources of data. That is information not collected for the explicit purpose of the research.[109] The great advantage of such data is that they already exist and thus research can be conducted more swiftly and cost-effectively than undertaking novel research or establishing new, large scale cohort studies.

To obtain enough data for a cohort of sufficient numbers of women, having had a hysterectomy, to generate meaningful and generalisable results, routinely collected data offered the most pragmatic solution in this project. However all routine health statistics are vulnerable to variable data quality and the subsequent risk of bias.[10] Additionally the lack of control over the data puts the researcher in a position where it may be impossible to validate the data they are using, whereas in novel research the researcher usually has a large degree of control over data quality and the choice of data items recorded.[109]

The three datasets chosen for extraction and subsequent linkage in this study each offered access to unique data items and the two national databases are known to be of high quality with rigorous quality assurance in place.[110;111] Other databases were considered including primary care databases i.e. the General Practice Research Database (GPRD)[112] which is the largest database of a longitudinal medical records, encompassing 4 million UK patients in approximately 500 GP surgeries.

Also considered was EPIC: an organisation which is responsible for international data (France, Italy, Germany, Belgium, Czech Republic and Australia with Korea and Spain) via Cegedim Strategic Data (CSD) and The Health Improvement Network (THIN), another longitudinal primary care database in the UK.[113] These data sources would have provided excellent data about co-morbidities and lifestyle of patients but were all rejected because Hospital Episode Statistics offered the most comprehensive detail about the hospital admission (operation and diagnostic detail) and the cervical screening database held the most reliable and comprehensive cytology call and recall data.

Hospital Episode Statistics

Hospital Episode Statistics (HES) is a national database of patient admissions and appointments in hospitals, in each of the devolved countries of the United Kingdom.[114] The data is collected by the individual NHS trusts and coded before being uploaded to HES. Chapter 3 includes further detail about the data held within HES and how it may be accessed.

The data held by HES has been created by data entry clerks or 'coders' based in every NHS Hospital in the UK. They classify each episode of hospital attendance and record precise details of: patient demographics, the date, type and location of the episode, diagnostic and treatment codes.[115;116]

The NHS Classifications Service 'delivers national clinical classifications standards and guidance for the NHS clinical coding profession'. They provide an education, training and formal accreditation programme for clinical coders and are developing a national clinical coding strategy alongside the Health Informatics Programme. It takes approximately two years for a person to become an 'Accredited Clinical Coder', and has its own Continuing Professional Development programme.

Thus the quality of the data recorded is regarded highly and is used as the basis of payments and funding as well as a valuable source of audit and research material.[117]

Cervical screening data – 'Exeter'

The suite of software which holds all cervical screening data in the UK has evolved from a programme called 'Exeter' and thus is colloquially known as such. Data are uploaded from Cytopathology laboratories around the country to regional 'hubs' and then finally collated to the 'Open Exeter' computer system which can be interrogated. Because there are several steps in the process there are several opportunities for the process to break down, however rigorous safety and back-up processes are in place and quality assurance systems in place to ensure data are recorded uniformly throughout the UK.[111]

Hospital histopathology records

Individual hospitals use various computerised databases to store information about their histopathological specimens. Typical (but not universal) information recorded includes patient identifiers (name, hospital number, NHS number, date of birth, address), sample identifiers (description, typographical and morphological codes, a sample unique number), dates of samples (when obtained, when received at lab, when processed or reported) and details of the clinician reporting the sample.

Unfortunately there is no NHS wide consensus on which software to use, or even on how to code specimens – some use free text coding, others use Systemised Nomenclature of Medicine (SNOMED) codes, or its one of its predecessors. Thus the choice of hospital laboratory data to supplement and validate the data from HES and Exeter was taken with caution as the quality of data that may be obtained was uncertain until it was received.

2.4.3 Record linkage

Record linkage encompasses the concept of collating disparate records, to generate new datasets, for a defined purpose.[118] Various techniques have been used over the past 40 years, which mirror the advances in routinely collected data systems.[118] There have been hugely complex systems devised to link data based on patient names or date of birth.[119;120]

One of the major decisions that impacts on the quality and completeness of any linked data, is whether or not data matching has to be perfect (all-or-none) or probabilistic (varying degrees of probability of a correct match). The advent of the new NHS number[121] as a personal, unique identifier has made data linkage far more accessible to researchers as, where it is used consistently and the validity of the NHS number is checked, then it provides the ideal linkage item and perfect matching can be the standard.[118]

For this study the two main databases (HES and Exeter) were known to contain NHS number as well as other highly specific identifiers (Date of birth and postcode) thus the study was designed to preserve patient confidentiality as far as possible by not using patient names at all. Thus linkage would be performed first on perfect matching of NHS number, and where this did not exist perfect matching of date of birth and postcode could be used as surrogate identifiers. The decision whether to include any probabilistic matching had to be taken at the stage of data collection when it became evident that a small number of minor (single integer) differences between records existed, thus a very limited application of this method was also used.

The use of postcode as a patient identifier is a well established identifier in linkage studies in the UK as the Royal Mail allocates a postcode to a group of no more than 80 properties.[122]

There are over 28 million postcodes currently valid in the UK[123], although for a research study is it theoretically possible to have neighbours from one street as participants and as such cannot be used as a unique identifier.

Date of birth is a useful identifier in small to intermediate sized population studies as, for a given population; there are thousands of possible dates of birth. However, with large datasets (>1,000 records) it becomes increasingly likely that date of birth will not be unique. When used in conjunction with other identifiers it is a very useful item as it is frequently recorded and allows for age to be calculated.

2.5 SUMMARY AND STATEMENT OF STUDY AIMS AND OBJECTIVES

Thus, the literature concerning hysterectomy is extensive, with references to this major operation being undertaken even prior to the advent of general anaesthesia. Incidence of hysterectomy has varied over time, at the time of writing, it is estimated that approximately 20% of women in the UK undergo a hysterectomy during their lifetime, however fewer operations are being performed each year as less invasive technologies are developed which reduce the requirement for major surgery and it is reasonable to assume that this lifetime incidence will gradually decline.

There are various methods of undertaking a hysterectomy; for the purposes of this study it is important to be mindful that a total hysterectomy involves removal of the uterine cervix, whereas sub-total hysterectomy does not.

Screening for pre-invasive disease of the cervix, using exfoliative cytology, has been highly successful in reducing the incidence of cervical cancer in those countries that have adopted it; the UK programme is one of the most successful in the world because it achieves full population coverage and has high uptake rates.

After a hysterectomy, follow up by the use of vaginal vault cytology is not recommended for the majority of women; only those whose histology reveals CIN at surgery or who have not had at least 10 years of screening prior to surgery should have further testing. These national recommendations are, of necessity, based on 'expert opinion' as little high quality evidence exists.

It has been suggested that some vaginal vault cytology is being undertaken inappropriately, particularly in primary care. Thus this study aimed to identify a cohort of women undergoing hysterectomy and consider their entire screening history both before surgery and subsequently, to establish if this suggestion is true and to quantify the problem.

A retrospective record linkage study was designed so that women having undergone a hysterectomy could be identified from routinely collected Hospital Episode Statistics and then their entire screening histories could be obtained from Open Exeter and merged. Supplementary data being obtained from individual histopathology laboratories, where possible. This design was chosen as being a pragmatic way to obtain the maximum amount of high quality routinely collected data within a relatively short period of time.

Thus the aims of this study were established as:

Primary: To describe the variation in both hysterectomy rates and subsequent follow-up by use of the vaginal vault cytology test, in the West Midlands region.

Secondary: To inform the development of national guidelines by generating high quality evidence of current practice with respect to vaginal vault cytology and assessing its appropriateness.

The study objectives were thus set:

Primary Objectives

- To estimate incidence rates for hysterectomy operations in the West Midlands region of the UK
- To describe variations in incidence of hysterectomy and establish those factors associated with variability
- To describe the current indications for hysterectomy in West Midlands
- To describe cervical screening patterns prior to hysterectomy
- To establish the current pattern of follow-up after total hysterectomy by means of vaginal vault cytology test
- To describe the results of vaginal vault cytology with respect to histology at hysterectomy and establish those factors associated with having an abnormal result
- To assess if vaginal vault cytology is being undertaken appropriately and establish those factors associated with inappropriate usage

Secondary Objectives

- To provide high quality evidence to inform national guidelines.

CHAPTER THREE: STUDY METHODOLOGY AND DATA SOURCES

INTRODUCTION TO CHAPTER

This chapter explains the development of the detail of the study protocol and justifies the chosen methodology with particular emphasis on the use of confidential patient data without explicit consent. The chapter then outlines the methodology used throughout the project, explores the three different sources of patient data and explains the various processes and approvals navigated to permit access to such confidential data. Details of how this data was securely stored and subsequently managed are also summarised. The chapter concludes with an overview of the planned statistical analysis and a justification of the statistical methods applied.

3.1 STUDY DEVELOPMENT AND ETHICAL APPROVALS

3.1.1 Developing the study protocol

To answer the initial research question of 'when should vault smears be undertaken?' it was necessary to consider a population of women who may be eligible to have a vault cytology test (vault smear) i.e. women who had their cervix surgically removed at a hysterectomy operation.

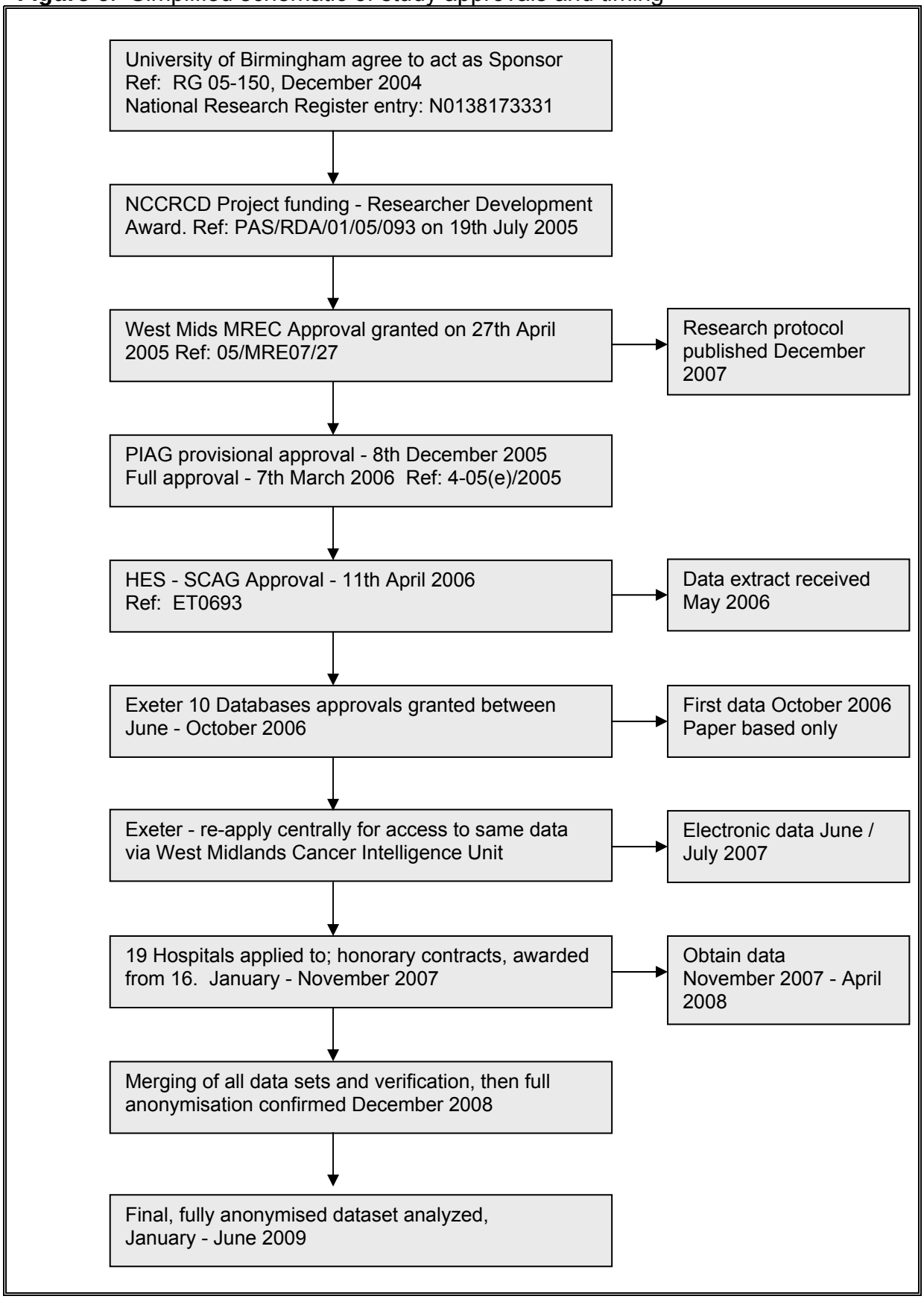
Thus it was necessary to identify a cohort of women having had a hysterectomy undertaken in a specified time frame and to establish the reasons for that surgery. Hospital Episode Statistics (HES) was the natural choice for access to this information (see section 3.2).

The West Midlands region was chosen as a good proxy for the whole of the UK population, representing 10% of England and Wales, or 11% of England,[124] with ethnic diversity second only to London.[125] It was predicted that this would provide almost 5,000 women who had a hysterectomy operation, generating a large enough sample to ensure that various subgroups could be studied further (see section 3.5.1 for sample size calculations).[126]

A woman's histology result following hysterectomy may not accurately reflect her cervical screening prior to surgery if she had colposcopic treatment in advance of definitive surgery. Thus it was important to access each patient's cervical screening history, for at least 10 years prior to hysterectomy. This data would be provided from the regional screening databases, colloquially known and hereafter referred to as 'Exeter' databases, of which, 10 represent the West Midlands population.

Finally, to add more sophisticated data about diagnosis at hysterectomy, to confirm that the operation included removal of the cervix and to validate the HES and Exeter data, some of the individual hospital pathology laboratories would have their data about the patients pathology results scrutinised.[127] Figure 6 summarises the study protocol in addition to all approvals.

Figure 6. Simplified schematic of study approvals and timing



3.1.2 Ethical issues arising from the use of confidential patient data without informed consent

Justification for not seeking individual patient consent: A key principle of the study was the necessity to access confidential, individual-patient data to allow for data 'linkage' to be performed between the different sources. This meant access to details of patient's unique NHS number, date of birth and postcode of home residence. Due to the large numbers of women in the study, individual patient consent could not pragmatically be obtained and so there were many necessary, and appropriate, ethics approval processes to be navigated before the study could commence data collection.

Historically, research ethics committees have had to consider all aspects of research applications to ensure that patient safety and dignity is preserved whilst supporting research activity within the NHS. However, after the Health and Social Care Act (H&SCA) 2001 was implemented, the Patient Information and Advisory Group (PIAG) took on the role of regulating researcher access to confidential patient information without individual patient consent.

Significant ethical issues arise from the decision to undertake any research that uses confidential information without involving the patient directly in the consent process.

The principle of obtaining informed consent prior to commencing research is commendable; however, some research has the potential to cause harm to the patient if consent is sought i.e. by revealing poor prognostic information or by contacting the seriously ill or approaching relatives of recently deceased patients. There is always a balance between potential benefits and harms; one of the key roles of research ethics committees is to weigh-up this decision-making process.

When conducting large scale, population studies, there are practical considerations that must also be considered; to contact and obtain informed consent from over 5,000 women would make this study prohibitively expensive, time consuming and ultimately impractical. Additionally, we know that people who consent to involvement in research trials are often not truly representative of the populations from which they are selected.[128;129] To generate research findings which are truly valid and representative of whole populations an adequately sized sample is essential.

Justification for specific data items: This study required several identifying items of data to allow for reliable data linkage to take place. The identifying items were chosen specifically to maximise predicted matching whilst minimising the degree of 'breach of confidentiality' i.e. patient's full name and address was not requested but postcode of home address, date of birth and NHS number were.

Postcode: This indicator, assigned by The Royal Mail to facilitate efficient mail delivery, is representative of an address block and includes up to 80 private addresses (usually less than half this number), anyone can access address details on supplying a postcode and so it is not a secure anonymous source. There are just over 1.5 million postcodes in use in the UK representing 27 million addresses, with some addresses having their own postcode (usually if their volume of post is in excess of 500 items daily i.e. businesses and large institutions).[123]

Date of birth: This indicator is not specific enough to use in isolation because, in a given area, many women will have the same date of birth, i.e. for women of childbearing age: 13 – 50 = 37 years x 365.25 possible days of year giving approximately 13,500 possible dates of birth. Although use of this indicator allows for age data to be subsequently calculated. When used in conjunction with postcode, date of birth is increasingly helpful as a patient identifier.

NHS Number: The new or modern NHS number comprises 10 digits. The first nine are the individual patient identifier and the tenth is a 'check digit' used to confirm the number's validity. The check digit is calculated using the Modulus 11 algorithm, Appendix C includes details of how this algorithm is applied: there are four steps in the calculation which is too complex to be verified without working through the process carefully.

NHS number can be used by any registered NHS employee to identify a patient by performing a straightforward electronic search. It is intended that every person in the UK should have their own, unique NHS number which is the link to their entire medical record.[121] NHS number has been, since 2002, allocated at birth, although for the women in this study most would have had their NHS number allocated during their lifetime when the NHS changed from an older system of NHS numbering during the late 1990's.[121] Although using NHS number is 'more' anonymous than a patient's name, it is still only represents 'partial' or 'pseudo' anonymisation.

Environmental impact: To minimise breach of individual patient confidentiality, and minimise paper waste, the study was designed to be 'paper light' i.e. to generate the minimum amount of paper wherever possible, and specifically not to generate any paperwork containing patient identifiable data. Because the project was based in a large university department it was not possible to calculate a project specific 'carbon footprint'. However, email and computer communication was used in preference to mailing; scanning and screen reading of documents undertaken as standard and travel was kept to a minimum.

Pseudo anonymisation stage: It was a condition of one of the approvals (section 3.1.6) that once initial linkage of data from HES and the Exeter cervical screening data had taken place, that data would be 'pseudo anonymised' to leave just NHS number as an identifier, so that when the data were taken from The University of Birmingham out to individual hospitals, the opportunity for breach of confidentiality would be minimised.

This was weighed against the inevitable reduction in data matching that could take place at hospitals by using just one indicator and deemed to be an acceptable compromise.

Full anonymisation and long term confidentiality: This was to be undertaken and verified once the data gathering was complete. Analysis could not begin until the data was fully anonymised. None of the outputs from this research can use any individual patient identifiers, thus ongoing patient confidentiality is assured. Appendix D includes a copy of the study System Level Security Policy which was developed in conjunction with the University of Birmingham Caldicott Guardian, information technology advisors and in line with guidance issued by the Security Advisory Group of HES.

3.1.3 Overview of all study approvals

The stages of necessary approvals are summarised in the flowchart: Figure 5. Appendices E1 – E5 contain a sample of the applications. Subsequent to the University of Birmingham agreeing to act as study Sponsor.

Approvals had to be sought from the following: Centre for Research Ethics (COREC, Appendix E1), now known as the National Research Ethics Service (NRES), the Patient Information Advisory Group (PIAG, Appendix E2), the Hospital Episode Statistics Safety and Confidentiality Advisory Group (HES, SCAG, Appendix E3).

Once the required data had been obtained from HES, then the ten local database controllers for cervical screening were approached for their permission to access data and obtain an extract. Appendix E4 includes an example of a letter of application. Finally, the 19 individual NHS hospitals in which hysterectomy operations were undertaken, had to be approached and the relevant consultant Histopathologists and their respective Research and Development (R&D) Departments' permission had to be sought for access to hospital data. Appendix E5 includes an example of one such application.

3.1.4 Prior approval: University of Birmingham willingness to act as sponsor

The University of Birmingham (UoB) has clear procedures with respect to applications for research ethics approval and research funding, to ensure that: research governance principles are followed; indemnity is in place to cover the study and appropriate accommodation and resources exist to support the research activity. This process grants a study ‘Confirmation of Sponsorship and Indemnity’ by the University’.

Subsequently the study was registered with the National Research Register Reference N0138173331[130] and although this resource is now archived, all studies registered with it are still available via the National Institute of Health Research (NIHR) National Research Register (NRR) archive.[131]

3.1.5 MREC approval

Ethical approval for the study was granted by West Midlands Research Ethics Committee via the National Research Ethics Service (NRES) of the National Patient Safety Agency (NPSA) of the NHS on 27th April 2005. Appendix E1 contains a copy of the application form and subsequent correspondence confirming ethical approval.

3.1.6 Obtaining Patient Information Advisory Group (PIAG) approval

Section 60 of the Health and Social Care Act (H&SCA) 2001 enables the Secretary of State to support and regulate the use of confidential patient information 'in the interest of patients or the wider public good'. Section 60[132] essentially permits the temporary setting aside of the ‘common law’ duty of confidentiality for the use of medical records for specific purposes. However, it does not set aside the requirements of the Data Protection Act 1998 (DPA98).[133;134]

Parliament agreed to the creation of this Act to ensure that any 'patient identifiable' information that was needed to support essential NHS activities could be used without informed patient consent, where there was no 'reasonably practicable alternative'. The Patient Information Advisory Group (PIAG) was established subsequent to the introduction of this Act of Parliament to manage the demand from researchers for access to this information.[135] Since 2008, an amendment to the Health and Social Care Act (2008) established a new statutory body, the National Information Governance Board for Health and Social Care (NIGB) to replace PIAG which was abolished on 31 December 2008.[136] However, for the purposes of this study PIAG was the body responsible for granting approval.

Acceptable use of patient data according to PIAG included: preventative medicine, medical diagnosis, medical research, provision of care and treatment, management of health and social care services, informing individuals about their physical or mental health or condition, the diagnosis of their condition or their care or treatment.[135] PIAG used to meet quarterly to review received applications and if there were practicable ways identified of gaining patient consent or using anonymised information, then an application would be refused.

Two main types of approval existed, namely 'class' and 'specific' support: 'Specific approval' was only ever granted for two areas: communicable disease and other risks to public health and also medical purposes related to the diagnosis or treatment of neoplasia i.e. activities carried out by cancer registries.

'Class support' was possible for a variety of activities and it was under this heading that permission was sought. Application was made to PIAG, in November 2005, under sections iv and v, see Figure 7.

Figure 7. PIAG rules for Class support

> *iv. To link patient identifiable information obtained from more than one source in order to validate the completeness or quality of the information or to avoid the impairment of the quality of the data by unintentionally including the same information more than once.*
>
> *v. To process patient identifiable information for the purpose of auditing, monitoring and analysing patient care and treatment.*

At first reading, PIAG recommended increased patient participation in the research project, despite user input into the study protocol and so INVOLVE,[137] a national advisory body which aimed "to promote and support active public involvement in NHS, public health and social care research", was contacted. INVOLVE believed that involving members of the public leads to research that is more relevant to people's needs and concerns, more reliable and more likely to be useful.[137] Essentially the organisation promoted the involvement of the public in the research process thus leading to improvement in the way that research is undertaken. However INVOLVE had no relevant groups based in the Midlands at the time of application and, although helpful and supportive of the project aims, they were unable to suggest ways of increasing user involvement beyond what had already taken place in the protocol development stage.

It was subsequently decided, with the support of PIAG, to publicise details of the research project throughout the West Midlands in freely available research publications. These were routinely distributed to healthcare organisations including GP surgeries, so that anyone (public or professional) could approach the author either for exclusion from the database (during the brief stage where data was identifiable) or for further information.

PIAG additionally stipulated that at the stage of requesting data from hospital histopathology laboratories, NHS number alone should be used as an identifier to minimise the opportunity for breaching confidentiality.

PIAG gave their full approval to the study, once these modifications had been incorporated, on 7th March 2006 - Ref: 4-05(e)/2005. Appendix E2 contains a copy of the successful application and relevant correspondence.

3.2 HOSPITAL EPISODE STATISTICS (HES)

3.2.1 Background: What is Hospital Episode Statistics Database (HES)?

Hospital Episode Statistics (HES) is a national database containing approximately 13 million records of patient admissions or appointments (episodes) for each 'data year' (1 April to 31 March) detailing the patient care that is provided by NHS hospitals in England.[138] Extracts from these data can be provided for any time from 1989 onwards. Data for NHS hospitals in Northern Ireland, Scotland and Wales are similarly collected and are available separately. Northgate Information Solutions is the independent company that manages the HES database.

Each HES record may contain over 50 items of information collected directly by hospital providers, including demographic details relating to the patient, diagnoses and surgical procedure codes. In addition, the central database provides a number of derived items from this supplied data i.e. using patient postcodes several indicators are added such as Super Output Areas (SOA) and Primary Care Trust (PCT) of residence.

To obtain an extract from HES that contains fields that potentially identify a patient or their hospital consultant then the application requires approval from the Security and Confidentiality Advisory Group (SCAG) at HES before it can be processed. This is to ensure that high standards of data security are in place and that the information is being used for legitimate, ethically approved research projects.

Once a request is approved by SCAG, the Department of Health authorises Northgate Information Solutions to proceed with producing the data extract, for which a fee is payable.

3.2.2 The data held in HES and applying for access to it

For each hospital episode, in addition to each patient's demographic and NHS registration details, data about the diagnosis that was attributed to the patient and the details of any procedures that were undertaken are documented in coded form. Every hospital consultant and GP surgery has a unique code which is recorded along with coded details of Heath Authority and Primary Care Trust of the patient and the organisation where they were seen. Dates of hospital admission and discharge and duration of stay are also recorded, making this a unique resource.

Any data that needs to be later retrieved and analysed first has to be summarised and coded. Various coding systems are in use in HES data to permit comparisons over time and against international standards. The data held by HES has been created by data entry clerks or 'coders' based in every NHS Hospital in the UK. They classify every episode of hospital attendance and record precise details of: patient demographics, the date, type and location of the episode, diagnostic and treatment codes.[115]

3.2.2.1 ICD 10 – An overview

The illnesses, diseases and injuries experienced by patients are currently recorded in HES using the International Statistical Classification of Diseases and Related Health Problems - Tenth Revision (ICD-10), published by the World Health Organization (WHO).[139] ICD-10 was endorsed by the Forty-third World Health Assembly in May 1990 and came into general use from 1994. The classification is the latest in a series which has its origins in the 1853, when the first international statistical congress was convened in Brussels by Dr William Farr, the Registrar General and Medical Statistician for England and Wales and has been steadily evolving ever since.[140] However, the first known 'modern' systematic classification of disease dates back to 1700: The London Bills of Mortality was an attempt to estimate the proportion of live born infants, who died before the age of six years, and it listed 13 classes of disease.

ICD-10 is presented as three volumes or divisions:

- the *tabular list,* including the actual classification at three and four character levels and classification of neoplasms
- the *instruction manual*, a collection of notes and historical material
- the *alphabetical index*[140]

Information about an individual patient's diagnosis at a very specific level, which has been recorded in their case notes by the clinician treating them, is later translated into ICD-10 codes by a 'clinical coder'. Thus it should be possible to compare conditions consistently, not only within HES but internationally, wherever ICD-10 is used.

Thus, ICD has become the international standard diagnostic classification for all general epidemiological and many health management purposes. It is used on many types of vital records including death certificates and hospital records. In addition to enabling the storage and retrieval of diagnostic information for clinical and epidemiological purposes, these records also provide the basis for the compilation of national mortality and morbidity statistics by WHO Member States.[139;140]

ICD-10 codes comprise a single alphabetic letter followed by two or more digits, with a decimal point between the second and third (e.g. *C53.1 Malignant neoplasm of cervix uteri, exocervix*). As there are many thousands of variations at the 4-character level (where all three digits are used) it is common practice to summarise at the 3-character level (e.g. *C53 Malignant neoplasm of cervix uteri*). Diagnosis tables are freely available for download at both the 3-character and the more detailed 4-character levels and are presented in code order.[139] Table 8 summarises the 'chapter headings'.

Table 8. ICD-10 Chapters

Chapter	Blocks	Title
I	A00-B99	Certain infectious and parasitic diseases
II	C00-D48	Neoplasms
III	D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
IV	E00-E90	Endocrine, nutritional and metabolic diseases
V	F00-F99	Mental and behavioural disorders
VI	G00-G99	Diseases of the nervous system
VII	H00-H59	Diseases of the eye and adnexa
VIII	H60-H95	Diseases of the ear and mastoid process
IX	I00-I99	Diseases of the circulatory system
X	J00-J99	Diseases of the respiratory system
XI	K00-K93	Diseases of the digestive system
XII	L00-L99	Diseases of the skin and subcutaneous tissue
XIII	M00-M99	Diseases of the musculoskeletal system and connective tissue
XIV	N00-N99	Diseases of the genitourinary system
XV	O00-O99	Pregnancy, childbirth and the puerperium
XVI	P00-P96	Certain conditions originating in the perinatal period
XVII	Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities
XVIII	R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
XIX	S00-T98	Injury, poisoning and certain other consequences of external causes
XX	V01-Y98	External causes of morbidity and mortality
XXI	Z00-Z99	Factors influencing health status and contact with health services
XXII	U00-U99	Codes for special purposes

The primary diagnosis in HES is defined as 'the main condition treated or investigated during the relevant episode of healthcare'. Where a definitive diagnosis cannot be applied then a code describing the main symptom, abnormal finding or problem is used. The HES database also stores up to 13 additional, 'secondary' diagnoses (only six prior to 2002-03), which describe other conditions the patient may have. The hospital will enter only codes necessary to describe the patient's condition, thus most records have far fewer than the maximum permitted 14 codes.

3.2.2.2 The UK classification of Operative Procedures (OPCS-4) and SNOMED CT.

An 'operation' usually comprises several separate procedures that, when put together, have a specific planned outcome (i.e. many operations involve making an abdominal incision but only hysterectomy operations involve excision of the uterus). Operations can be relatively simple or very complex, there are different ways in which a named operation can be performed, such as using endoscopic surgical techniques. These different aspects of each operation are currently recorded separately in HES using the UK Classification of Operative Procedures (OPCS-4).[141]

HES records store up to 12 OPCS-4 codes recorded for each episode, (four prior to 2002-03). The 'main operation', which is the first one listed in a HES record, is normally the most resource intensive procedure performed. Any additional OPCS-4 codes (where they occur) are known as 'secondary procedures'.

OPCS-4 codes consist of a letter followed by three figures. The letters denote the 23 'chapters' of the classification; each chapter dealing with a different part, or 'system' of the body. There are around 6,000 codes available but for many purposes it is acceptable to group codes at the 3-character level. However, where more precision is required the sub-division indicated by the final character adds further detail; a point is used to separate the 3-character 'group' code from the final integer, i.e. *Q01 = Excision of cervix uteri,* but for more detail *Q01.3 = Excision of cervix uteri, Excision of lesion of cervix uteri*.

Data is freely available at the 3 and 4-character levels, providing counts of main operations.[141] Table 9 gives the name of each of the chapters; for the purposes of this study chapter Q, the upper female genital tract, is where hysterectomy operations are classified.

There is an alternative newer coding system called SNOMED CT® which is currently being developed and it is envisaged that this will supersede OPCS (and several other classifications) in the next few years, however currently OPCS is the NHS standard. SNOMED CT is a clinical terminology - the “Systematised Nomenclature of Medicine”.

Table 9. OPCS Chapters

Prefix	Chapter	Prefix	Chapter
A	Nervous System	N	Male Genital Organs
B	Endocrine System and Breast	P	Lower Female Genital Tract
C	Eye	Q	Upper Female Genital Tract
D	Ear	R	Female Genital Tract associated with pregnancy, childbirth and puerperium
E	Respiratory Tract	S	Skin
F	Mouth	T	Soft Tissue
G	Upper Digestive Tract	V	Bones and Joints of Skull and Spine
H	Lower Digestive Tract	W	Other Bones and Joints
J	Other Abdominal Organs	X	Miscellaneous Operations
K	Heart	Y	Subsidiary Classification of Methods of Operation
L	Arteries and Veins	Z	Subsidiary Classification of Sites of Operation
M	Urinary		

SNOMED CT It is a common computerized language that will eventually be used by all computers in the NHS to facilitate communications between healthcare professionals in clear and unambiguous terms. It will be the language of the NHS Care Records Service and will reduce potential for differing interpretations of information and the possibility of errors resulting from traditional paper records.[142]

SNOMED CT was a joint development between the NHS and the College of American Pathologists (CAP) to improve and safeguard patient care by using an agreed terminology. It has greater depth and coverage of healthcare than the current systems that it is planned to replace.

Great efforts are being made to ensure that older codes will be accurately translated into SNOMED CT when the changes are rolled out so that valuable, historic data will not be 'lost'. It should, ultimately, enable clinicians, researchers and patients to share and exchange healthcare and clinical knowledge worldwide.

In April 2007 the International Health Terminology Standards Development Organisation (IHTSDO) acquired the intellectual property rights of SNOMED Clinical Terms (SNOMED CT). By acquiring the SNOMED CT standard the IHTSDO will help to ensure the continued maintenance and evolution of SNOMED CT as well as its availability on an international scale.[142]

3.2.2.3 Consultant codes

This comprises an individual Consultant's General Medical Council (GMC) registration number and as such can be used to identify each specialist individually by cross-referencing against the GMC website.[143]

3.2.3 The Security and Confidentiality Advisory Group of HES

3.2.3.1 Applying to The Security and Confidentiality Advisory Group (SCAG)

A written application was submitted to Northgate Information Solutions SCAG in early December 2005. However, the headquarters of this organisation are based in Hemel Hempstead and the, now infamous, fire at Buncefield Oil Depot destroyed their offices on 11th December 2005.

The application was re-submitted in January 2006 and by 23rd February 2006 a preliminary decision was reached. Impressive testimony to their back-up disaster planning that it took so little time. Full approval was granted on 11th April 2006. (Appendix E3).

3.2.3.2 Study 'Security Policy'

SCAG stipulated that the study should have a clearly defined 'security policy', including explicit consent from the Caldicott Guardian at The University of Birmingham. This necessitated getting specific approval from the University of Birmingham Data Controller: Dr Carolyn Pike, Director of Legal Services and University Data Protection Officer, who assumes the role of Caldicott Guardian when necessary.

A comprehensive system level security policy (SLSP) was drawn up (Appendix D), which defined standard practices to secure all patient identifiable electronic data used by the study. A specified security manger was named as were all persons who may have access to confidential data.

In summary, the only electronic format which would contain patient identifiable data would be one stand-alone lap-top computer with an associated external hard drive. These would both be password protected and their confidential data encrypted. When not in use they would be stored in a locked cupboard, located in a locked office in a secure department. The wireless networking capacity of the lap-top was disabled and regular internal audit arrangements were put in place.

Disaster recovery processes were also implemented with bi-weekly back-up copies (also password protected) of any new or changed data being created and stored in a fire-proof safe that was physically remote from the study office. It was planned that when patient identifiable data was removed from the hardware, supervised 'secure wiping' would be undertaken and signed off accordingly.

The data extract was received from HES in May 2005 and consisted of a single disc containing text files.

3.3 'EXETER' AND THE NATIONAL HEALTH SERVICE INFORMATION AUTHORITY

Cervical screening by means of the Papanicolaou cytology test was introduced ad hoc throughout the UK during the 1970s but only became a nationally co-ordinated, standardised, scheme in the late 1980s (see Chapter 2). The 'Exeter' suite of software was developed to manage the 'call and recall' of women in this first national screening programme. It has evolved significantly over time but colloquially remains known as 'Exeter' and will be referred to as such hereafter.

3.3.1 Background: What is 'Exeter' / The NHSIA?

The NHS Information Authority (NHSIA) was a 'special health authority' formed in 1999 to develop and deliver national information technology services to the NHS. The NHSIA ceased activity on 1st April 2005 and its work was taken over by two other organisations: NHS Connecting for Health and the Health and Social Care Information Centre.

NHS Connecting for Health is the organisation responsible for supporting the NHS computer programmes, systems and networks. Thus it covers a wide range of services and resources in primary and secondary care.

These include: referral systems (Choose and Book), Records (NHS Care Records Service) imaging storage and transmission (Picture Archiving and Communications System, PACS) the NHS Strategic Tracing Service plus new regional programmes for information technology. The NHS Strategic Tracing service (NSTS) is a database of all the people and NHS organisations within the NHS which can be searched. One of their objectives is to provide up to date NHS numbers on patients.

The Health and Social Care Information Centre describes itself as *"the leading provider of information for health and social care".* It was formed from the merger of some aspects of the NHSIA and the former Department of Health 'Statistics Unit' and they aim 'to be the leaders in collecting, analysing and distributing facts and figures for the various health and social care communities in the UK'.[144]

As these organisations have evolved, the cervical screening data remains and has passed through various different versions of software. Currently, cervical smear screening data is still held in multiple 'stand alone' databases which then download their information to regional cancer registries. Ten of these databases cover the West Midlands region and Appendix F summarises their details. At each site, a named 'Data Controller' can allow access to the information held therein and allow certain outputs to be created. These outputs include reports of full screening histories on selected cases, which may be searched for by various means, including NHS number, postcode and date of birth (although not all three simultaneously). However, these reports can only take the form of printed documents, and as such, for research on the scale planned this would not have been a suitable outcome.

3.3.2 Open Exeter

'Open Exeter' is a remote access, highly secure, system for accessing the 'Exeter' databases across the national network. The West Midlands Cancer Intelligence Unit (WMCIU) has permission to use the Open Exeter system to extract cervical screening records and so it is possible, if an individual obtains permission from each database controller individually, to access screening data electronically. However, this system is relatively new and obtaining permission is notoriously difficult.

It took 12-months to obtain all the necessary permissions to access data via Open Exeter, but permission was finally granted in June 2007 with data collection undertaken throughout June and July 2007. An example of an application is in Appendix E4.

Data was extracted by searching the database in batches of up to 40 records at a time, using NHS number alone (See Chapter 4 for further explanation). For some women, their NHS number or other records were in the system but they had no cytology test results recorded. Their demographic details were downloaded and saved separately from the main database. Many of these were women, born before 1/1/1923, were never routinely called to the national cervical screening programme (i.e. they were over the age of 60 by the time of the first national call).

3.4 LOCAL HOSPITAL HISTOPATHOLOGY AND CYTOPATHOLOGY DATABASES

There are 19 hospitals that have access to histopathology laboratories which process and analyse cervical cytology and gynaecological specimens, in the West Midlands Strategic Health Authority area. Each of these was approached for permission to undertake the third stage of data collection. Full permission was ultimately granted from 15 with two refusing outright and two asking for application to be deferred due to staffing problems. However data collection actually took place at just four sites as the value of this data source was called into question during the course of the study (Chapters 4.6 and 5.4).

3.4.1 The role of pathology laboratories

Hospital pathology laboratories are responsible for receiving organic samples, then cataloguing, processing, analysing and reporting them in a consistent, valid and reproducible way. There are very strict quality assurance systems in place in all NHS laboratories, which are accredited nationally via Clinical Pathology Accreditation (CPA) and the National External Quality Assurance Schemes (NEQAS) as well as via strict internal audit and quality control.[145] There has, historically, been great variation in investment in pathology services and although steps are being taken to standardise laboratories and their computerised systems this is still far from ideal.[146]

3.4.2 Access to histopathology laboratory data

Table 10 includes details of all the hospitals in the West Midlands that hold histopathological specimens from hysterectomy operations; these were all approached for access to their computerised records. The response from each is also summarised. Details, of a typical application, is available at Appendix E5. Hereafter discussion about hospitals will be anonymised to preserve confidentiality of patients and clinicians.

The various laboratories used several different IT systems to store and manage their samples. This raised concerns about how comparable data was going to be. However, consistent across all databases were the presence of some patient identifying items including full name and date of birth. Unfortunately, it transpired that NHS number was not used consistently, despite a clear intention to do so (all included it in their database).[145] Thus, because of the stipulation by PIAG that only NHS number could be used to identify patients at hospital level, (a form of pseudoanonymisation), the study had no access to patient names to facilitate more effective linkage of the hospital's data.

A major difficulty was that clinical coding of the samples across hospitals used several different systems: either various versions of SNOMED or its predecessor, SNOP (Systemised Nomenclature of Pathology). Unfortunately these different coding systems were not comparable for the purposes of this research. See chapters 4.6 and 5.4 for further discussion.

Table 10. Summary of hospitals in West Midlands region approached for data

Hospital & NHS Trust *(alphabetical)**	**Notes and decision**
The Alexandra Hospital, Worcestershire Acute Hospitals NHS Trust	Permission granted and full R&D approval.
Burton Queens Hospital NHS Trust	Consultant on long term sick leave, no-one covering her work, no-one able to give permission.
City Hospital NHS Trust	Full R&D and laboratory approval granted.
University Hospitals Coventry & Warwickshire NHS Trust	Cost issues a worry as grossly understaffed and funded, but 'happy to be involved in research if guaranteed no cost to the laboratory'.
George Eliot Hospital NHS Trust	Consultant on maternity leave until June 2008, no-one to cover or give permission.
Heartlands Hospital, Heart of England NHS Foundation Trust	Full approval granted which incorporated Solihull and Good Hope under one new NHS trust but two laboratories.
Hereford County Hospitals NHS Trust	Full permission granted after attending their R&D meeting in person.
Good Hope Hospital NHS Trust	Very helpful, full agreement, however lead consultant retired during the study. Full R&D and laboratory approval granted.
New Cross Hospital, Royal Wolverhampton Hospitals NHS Trust	Full R&D and laboratory approval granted.
University Hospital of North Staffs NHS Trust	Full R&D and laboratory approval granted.
The Princess Royal Hospital, Shrewsbury & Telford Hospital NHS Trust	Full R&D and laboratory approval granted.
Russell's Hall Hospital, Dudley Group of Hospitals NHS Trust	Informal permission granted swiftly; R&D approval delayed but granted.
Sandwell District General Hospital	Full R&D and laboratory approval granted.
Shrewsbury and Telford Hospital NHS Trust	Lead Histopathologist agreed, said no other permission needed but as part of same trust as Princess Royal, full R&D approval was granted.
Staffordshire General Hospital, Mid Staffordshire General Hospitals NHS Trust	Full R&D and laboratory approval granted.
Walsall Manor Hospitals NHS Trust	Full R&D and laboratory approval granted.
Warwick Hospital, South Warwickshire General Hospital NHS Trust	Head of Department not interested, declined further discussion.
Birmingham Women's Hospital, Birmingham Women's Healthcare NHS Trust	Full R&D and laboratory approval granted.
Worcester Royal Hospital, Worcestershire Acute Hospitals NHS Trust	Permission granted via lead Histopathologist. Full R&D approval later granted via The Alexandra hospital (one trust).

** NB Study results are presented anonymously, study numbers do not relate to alphabetical order*.

3.5 ANALYSIS PLAN

This study collated routinely collected data from multiple sources, as has been described. Hospital Episodes Statistics database initially provided details of all women who underwent a hysterectomy operation in the West Midlands region during 2002-03, their hospital coding for diagnosis, operations undertaken and comprehensive details of the admission. The 'Exeter databases' provided their entire cervical screening histories and any vault cytology data and the hospital laboratories provided some supplementary information about diagnosis.

3.5.1 Sample size calculations

This was to be a pragmatic sample of all women in the West Midlands region who underwent a hysterectomy operation in a specified time period thus there was no control over the size of the cohort, other than to use a longer time frame. However, sample size (power) calculations were undertaken during the protocol development to ensure the study would have sufficient power to detect important differences.

The key groups of women for analysis would be specified by their main histology result at the time of surgery (benign disease / cervical intraepithelial neoplasia (CIN) / malignancy) as this would determine their recommended follow up post-operatively by means of vaginal vault cytology tests, according to national guidelines.

Table 11 was used to provide the estimated proportions on the basis of previous research by the authors.[28]

Assumptions:

- 4,500 hysterectomy operations performed annually in West Midlands region[147]
- 80% of hysterectomies undertaken for entirely benign indications[1]
- 10% for CIN[2]
- 5% for cancer[2]
- 5% would be sub-total hysterectomy operations (any cause) and will thus be excluded from final analysis concerning vaginal vault cytology as the cervix would remain and so screening should continue according to national cervical screening guidelines (approximately 225 cases excluded).[28]

For the benign histology group, a sample of 1,800 women would be sufficient to estimate prevalence of follow up to within +/-1% (95% CI); for the CIN and cancer groups the estimate would be to within +/-4% (95%CI). Thus the anticipated sample would be more than adequate and did not need to be expanded further.

Table 11. Estimated numbers of women in each histology category for sample size calculations

	Sub-Total* *(Excluded)*	**Benign**	**CIN**	**All Cancers**	**Totals**
Not followed up by vault cytology (controls)	*N/A*	3,240 90%	90 20%	23 10%	3,353
Followed-up by vault cytology (cases)	*N/A*	360 10%	360 80%	202 90%	922
Totals	*225* *5%*	3,600 80%	450 10%	225 5%	**4,275** **(95%)***

** with 5% excluded from calculation as sub-total hysterectomy operations.*

3.5.2 Overview of planned analysis

Details of statistical tests actually used at each stage of analysis are provided in the results section (Chapter 6) along with the results obtained. Appropriate statistical tests were determined after assessment of data distribution and sample sizes and the choice of test affirmed by a statistician. Figure 8 summarises the planned analysis in a visual format.

Descriptive data was generated using queries in Microsoft Access 2003® SP2 and using Pivot Tables in Microsoft Excel 2003® with some descriptive work and all further statistical analysis undertaken using SPSSv15. Descriptions typically included mean (with standard error) for normal data or median values with ranges and interquartile ranges and an assessment of skewness for non-normally distributed data, confidence intervals of proportions were calculated and presented where relevant.

3.5.3 Justification of statistical methods

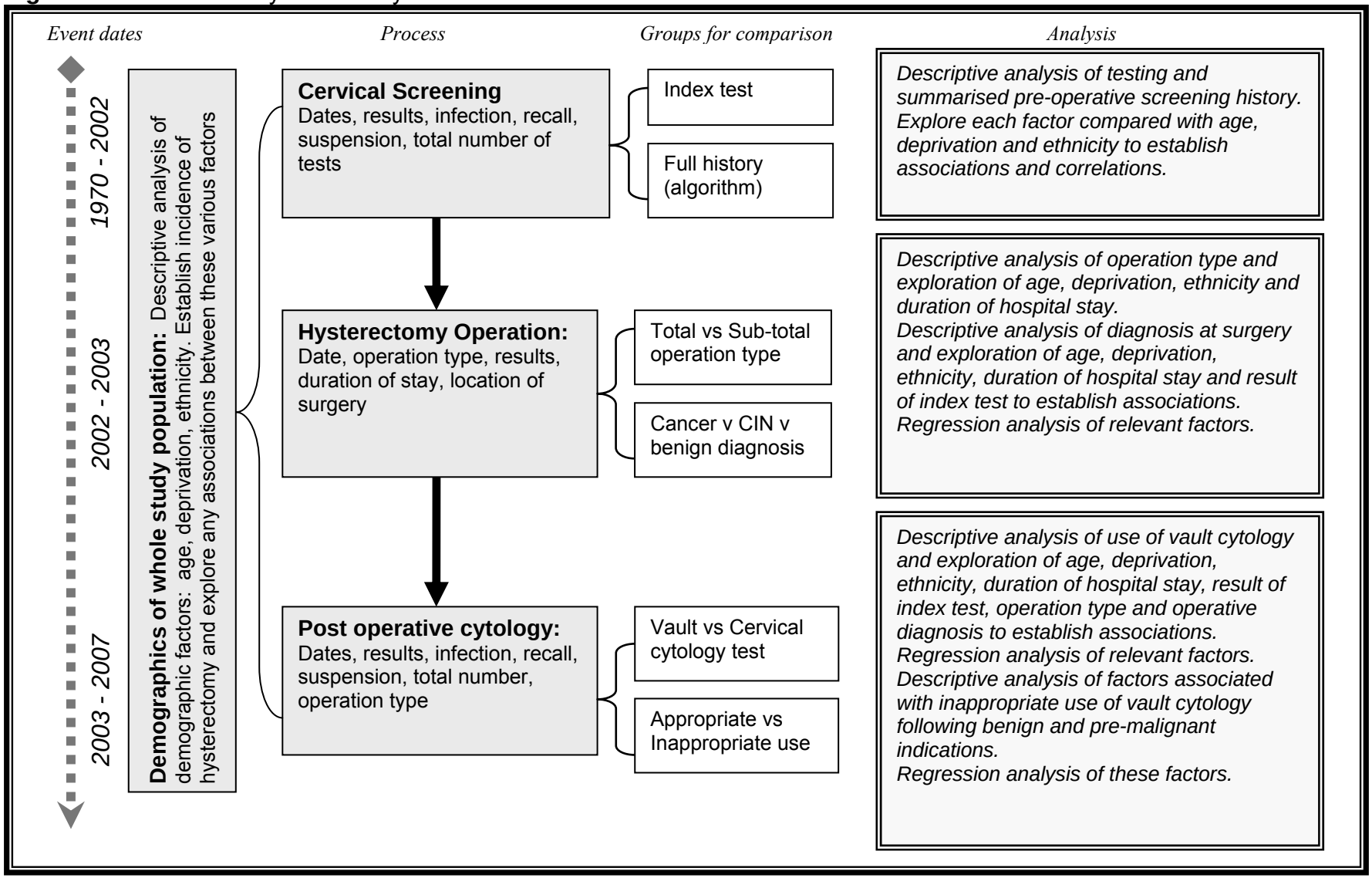
The data was analysed in four main sections and presented in tabular, graphical and text format as appropriate. The Kolmogorov-Smirnov test for normality was applied to establish if data was normally distributed, where relevant. Table 12 summarises the main statistical tests used in the analysis.[148]

3.5.3.1 Which women had hysterectomy operations?

Demographic factors were explored: Comparison of the whole study population against the West Midlands and England populations with respect to age, Index of Multiple Deprivation 2007 (IMD07) and ethnicity was undertaken initially and the results tabulated. Age was divided into five-year bands and ethnicity into six key groups (and later dichotomised) to permit meaningful comparisons and deprivation split into quintiles. Cross tabulations were undertaken for the various groups and χ^2 test applied with degrees of freedom (df) and significance values (p) stated.

Incidence rates for hysterectomy were calculated using population data (2001 census data). The numbers of screening tests undertaken were explored then divided into cervical tests pre-operatively and post-operatively (vault and cervical).

Figure 8: Planned Analysis of study database



3.5.3.2 Why did women have a hysterectomy operation? Cervical cytology results prior to surgery

Pre-hysterectomy cervical cytology data was explored with respect to age, deprivation and ethnicity. The last test before hysterectomy was explored in some depth, the 'Index' test, and women were divided by their result at this test into four main groups (cancer, dyskaryosis, normal or other). Comparisons were then made between the groups in terms of age, deprivation and ethnicity using Kruskal-Wallis χ^2 as the non parametric equivalent to a one way analysis of variance (ANOVA). Correlation between increasing age and increasing number of tests pre-operatively was assessed using Spearman coefficient.

The Wilcoxon signed ranks test was used to compare distributions of predicted total numbers of tests, by age band, against actual distribution observed, as this was an example of comparing differences in paired observations.

All the pre-operative screening data was coded according to 'per protocol' and 'non-protocol' patterns using an algorithm constructed by the cancer registry in the West Midlands (see Chapter 4.4 for further explanation); this was to ensure standardised results to facilitate future analysis and collaboration. Using this complex classification, women were further grouped into those having had a history of entirely normal screening or various combinations of abnormal cytology with two variations of sub-classification applied: a 13-group and a 4-group coding, to permit different types of analysis. This permitted comparisons between groups with respect to age at surgery, deprivation score and ethnicity.

3.5.3.3 What happened at hysterectomy? The surgical diagnosis

The reasons for hysterectomy were explored, with the diagnosis, obtained from HES records, being used as a proxy for reason for surgery. The diagnosis was explored with respect to deprivation score, age, ethnicity, index cytology test result, duration of stay and overall cervical screening pattern. Each of these was considered further by histology type: benign, CIN (further subdivided into CIN I, II & III) and malignant.

Regression analysis techniques are usually applied where statistical associations exist, to predict the value of one variable from knowledge of the others. Multivariate logistic regression analysis (where there are several variables in the model) was undertaken to establish if any factors were associated with type of hysterectomy operation (total or sub-total).

The first stage was formulation of a baseline model which took no account of any association among the variables (Step 0 in SPSS outputs). It provided a comparison for the evaluation of the final model. The backward likelihood method of regression analysis was undertaken because variables were selected which were predicted to be responsible for the observed outcome. This model gradually removed variables which were not actually associated, until the final model was obtained.

Table 12. Summary of main statistical tests used during analysis[148]

Statistical Test	Data Type	Example of use	Notes
χ^2	non parametric	Comparison of study population deprivation with reference populations or proportions of each ethnic grouping	To compare associations between rows / columns. Degrees of freedom must be stated
Kolmogorov-Smirnov test for normality	continuous	establishing if distribution of age in study population was normal	
Spearman rank correlation	continuous	Used to establish if a relationship exists between two continuous variables	
Kruskal-Wallis χ^2 Test	non parametric	To detect associations between a non normally distributed variable and a categorical one i.e. ethnicity and age	The non-parametric alternative to a one way ANOVA
McNemar	non-parametric	Test for equal proportions of index smear result compared with diagnosis at surgery	Test for agreement in paired data
One way ANOVA	parametric test	Result of index test compared with age	
Wilcoxon signed rank	non parametric	Distribution of expected tests per age band compared with observed distribution	The non-parametric alternative to a paired t-test
Pearson χ^2	non-parametric	Deprivation quintiles compared with operation type	
Logistic regression analysis: backwards, stepwise	non-parametric	To establish a model for predicting factors associated with having inappropriate vault cytology subsequent to hysterectomy for benign indications	Backwards method used where variables are predicted to be important in the final model

The analysis was also planned to be run in a forward fashion, to act as a check that any findings were valid and the most appropriate was reported. Nagelkerke R^2 is a measure of the 'goodness of fit' of the regression analysis model and was reported for all regression analysis. It is a modified variant of the Cox and Snell R^2 which can, by definition, never reach a correlation of 1, whereas the Nagelkerke R^2 can reach 1 and as such is now a favoured means of reporting regression analysis in SPSS.[149]

3.5.3.4 Post operative follow up: vault cytology or no vault cytology?

The numbers of women, of each histology type, having some follow up by means of a vault smear test subsequent to their surgery were described, again with respect to their age bands and deprivation scores.

Multivariate logistic regression analysis was then undertaken on those women who were followed up by means of post operative vault cytology and those who were not (binomial). This was to determine those factors, in addition to histology or operation type, that influenced whether or not a woman was followed up in this way.

3.6 SUMMARY OF CHAPTER

Chapter three has explained the overall study methodology and given prominence to ethical concerns about use of confidential patient data without consent.

HES was chosen to provide the data about hospital admissions as it is an established, high quality national data resource and uses the internationally accepted ICD10 diagnostic coding and OPCS4 operative coding.

The 'Exeter' software, used to record cervical screening history for the UK population, was interrogated to provide screening histories for the study population as it is the only national repository of screening data. Access to this data was eventually obtained via the West Midlands Cancer Intelligence Unit where the 'Open Exeter' system could be accessed.

Hospital histopathology data was found to be problematic, as the various hospital laboratories use widely different software to record their data. Although 19 hospitals were approached and permission granted from 15, data was eventually only retrieved from four.

The order of the statistical analysis and presentation of the results has been outlined along with justification of the statistical tests to be applied. These results will be presented in chapter 6.

CHAPTER FOUR: DATA EXTRACTION, LINKAGE AND ANONYMISATION

INTRODUCTION TO CHAPTER

This chapter considers the various processes involved in obtaining and managing the preliminary data, preparing it for linkage, the actual data linkage process and then subsequent anonymisation. These stages followed a logical progression and as such the chapter is process orientated. Boxes and flowcharts are used to guide the reader through the various stages and to facilitate understanding whilst attempting to avoid excessive use of technical jargon or formulae. Appendices G and H contain supplementary information.

4.1 DATA FROM HOSPITAL EPISODE STATISTICS (HES)

The HES data extract was supplied by Northgate Information Solutions, as two 'pipe delimited text files', see example Figure 9, essentially data items separated by a 'pipe' or '|'. These were uploaded, on receipt, to a securely password protected laptop computer, which had its wireless networking capability disabled. Then the files were converted into Excel spreadsheets, with columns separating the data items.

Figure 9. An anonymised (#) example of two records from the HES files

```
########|Z|#########9|2|08082002|13082002|19|502|502|1|C541|M801||||||||||||09082002|0908
2002||||||||||1|Q074|Q221||||||||||4|RXK01|00CSFY0021|00CSFY|06CSFY|5MJ|WS##
###|5MX|Y07|Q27|C#######|M88007|29707326
########|Z|########2|2|09052002|17052002|19|502|502|1|C541|M801||||||||||||10052002||||||||||
1|Q074||||||||||7|RXK01|00CSFF0013|00CSFF|06CSFF|5MJ|B##
###|5MX|Y07|Q27|C#######|M88007|29669254
```

4.1.1 Summary of HES Data

Full detail of the data validation process is included throughout Chapter 5; however Table 13 gives a summary of all the supplied items for each participant and a brief explanation of each.

4.1.2 HES Data preparation prior to obtaining cervical screening histories

Searching the 'Exeter' database system, which holds cervical screening data, for the records required in this study, using NHS number alone was recommended by local data controllers as being the most efficient technique. The Exeter databases were originally developed for internal use and were not designed to facilitate external audit, as such data search facilities are strictly limited to certain combinations of input data and certain formats. Due to the confidential nature of the data, clear guidance exists which specifies that 'no programming may be undertaken by external researchers'.

Table 13. Summary of supplied HES data items (operation data)

No.	Code	Explanation
1	DOB	Date of birth
2	ETHNOS	Ethnic group of patient
3	NEWNHSNO	New NHS number
4	SEX	Gender
5	ADMIDATE	Date of admission to hospital
6	DISDATE	Date of discharge from hospital
7	DISDEST	Discharge destination (i.e. home or another hospital)
8	MAINSPEF	Speciality of consultant
9	TRETSPEF	Treatment speciality of consultant
10	EPITYPE	Type of admission (general or obstetric)
11 - 24	DIAG01 - 14	Diagnosis ICD10 (International Classification of Diseases 10th revision) code - up to 14 per admission
25 - 36	OPDATE01 - 12	Date of operation - up to 12 per admission
37	OPERSTAT	Whether or not an operation was carried out
38 - 49	OPERTN01 - 12	Classification of Surgical Operations and Procedures (OPCS4) code - up to 12 per admission. OPERTN01 should be the main operation
50	POSOPDUR	Number of days in hospital after main operation
51	SITETRET	Hospital where operation conducted
52	OACODE	Super output area of residence
53	OACODE6	Shortened super output area of residence
54	WARD91	Electoral ward of residence
55	RESPCT	Primary Care Trust (PCT) of residence
56	HOMEADD	Patients home postcode
57	PCTTREAT	PCT where treatment occurred
58	ROTREAT	Region where treatment occurred
59	STHATRET	Strategic HA where treatment occurred
60	CONSULT	General Medical Council number of the responsible consultant
61	GPPRAC	General Practitioner surgeries code
62	EPIKEY	A unique record identifier created by HES

A ‘batch search’ facility may be employed in Exeter, where more than one NHS number can be searched for concurrently, the resulting output is a full record for each woman. To undertake these batch searches NHS numbers had to be converted to a defined format; 'Comma Separated Variable' or CSV files (Figure).

There were 5,882 NHS numbers listed from 6,168 records in the original HES database, however a few were duplicated: to identify the duplicate entries a simple Excel formula was used (Figure 10).

Figure 10. Excel formulae used in preparation for data extraction

To produce a comma delimited or 'comma separated variable = CSV' file:
Text: make this cell the same as NHS no but add a comma afterwards
Code version = A#&","

To identify duplicate entries where only small numbers of duplicates are predicted:
Text version: if cell in this row contains ‘NHS no’ which is identical to 'NHS no' in cell directly above, then copy the NHS number to a new column, if not leave new column blank. Then sort column to visualise all duplicate NHS numbers.
Code version: =IF (A#=A#-1,B#)

To identify duplicate entries where larger numbers of duplicates are predicted:
Text version: as above but then repeat formula in a new column as many times as needed to extract all duplicates.
Code version: as above.

Handling of 'Duplicate Entries'

46 NHS number entries were present more than once, with 19 instances of two records, one instance of three entries and one instance of five entries for that NHS number. The additional entries were identified and removed from the list of NHS numbers to be used for Exeter matching, to prevent duplication of record extraction.

This left 5,857 unique NHS numbers for matching and 26 lines of data referring to a person already eligible for matching. These cases fell into several categories and are identified in Table 14. The various types of duplicate are as follows:

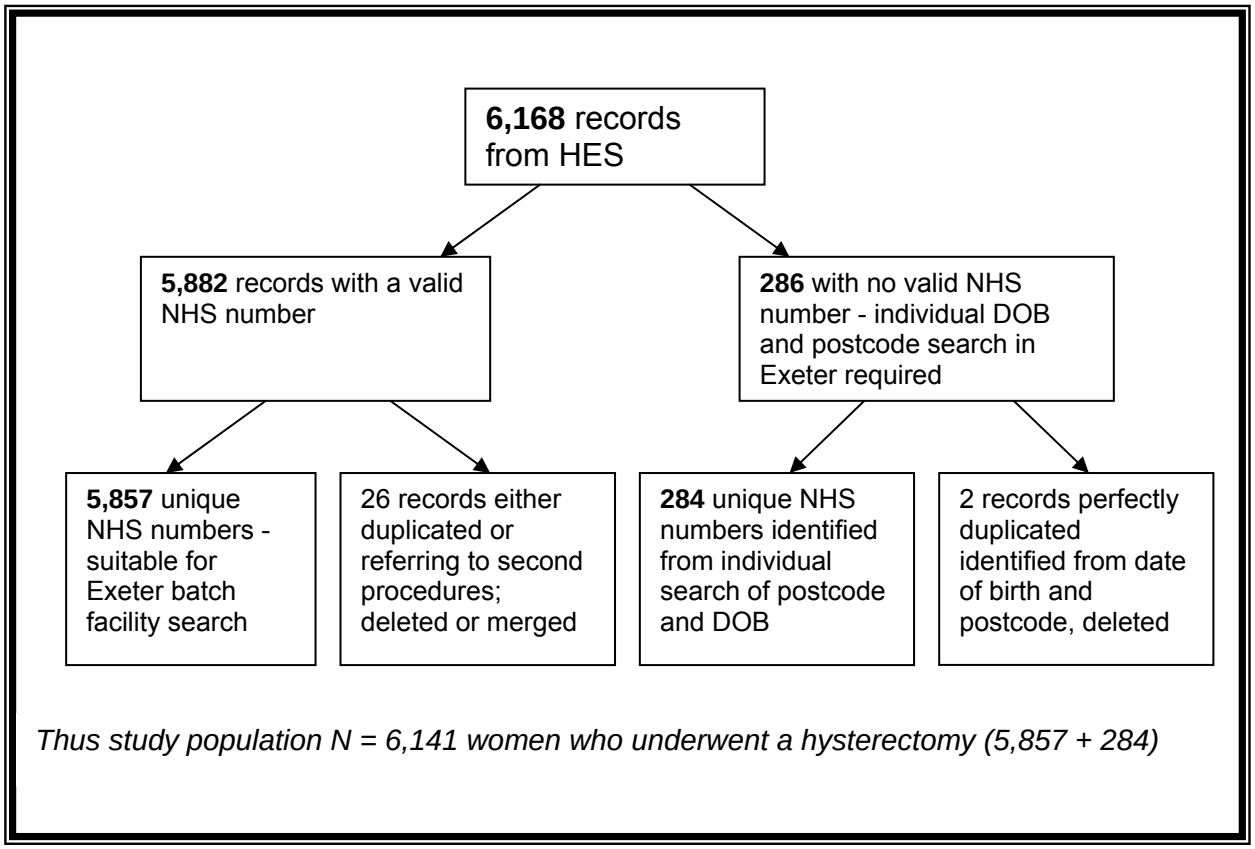
- Those for whom there was an entire identical duplicate entry but with two HESIDs applied: perfect duplicate.
- Those that referred to the same admission but were not identical entries: imperfect duplicate.
- Cases where a woman had more than one operation during her one hospital admission: one admission, more than one operation.
- Those that referred to more than one admission but where both were coded as a hysterectomy (greater than a month apart): two admissions.
- Those where the woman was re-admitted within a short space of time (less than one month) after surgery, most likely as a result of operative complications: re-admission.

For the duplicated records, given the small numbers a decision was made on the validity of each record individually, however, certain rules were applied consistently. Essentially in the case of perfect duplicates one record was deleted, for imperfect duplicates the most informative data line was retained or where totally different sets of codes were used the different data was collated (as the differences only applied to operation and diagnosis codes), for more than one admission the main procedure (including a hysterectomy) was be taken as the index record. A simple code was added to the file to this effect). Figure 11 demonstrates this process.

Table 14. Identification of type of duplicate records

NHS No.	No entries	Reason
4#######75	2	Perfect Duplicate
4#######68	2	Perfect Duplicate
4#######93	2	Perfect Duplicate
4#######62	2	Imperfect Duplicate
4#######59	2	Re-admission
4#######79	2	2 Admissions
4#######99	2	Perfect Duplicate
4#######43	2	2 Admissions
4#######08	5	1 Admission, >1 Op
4#######45	2	1 Admission, >1 Op
4#######90	2	Re-admission
4#######74	2	1 Admission, >1 Op
4#######53	2	Imperfect Duplicate
6#######73	2	2 Admissions
6#######01	2	Imperfect Duplicate
6#######04	2	2 Admissions
6#######49	3	1 Admission, >1 Op and 1 Perfect Duplicate
6#######98	2	Perfect Duplicate
6#######14	2	Imperfect Duplicate
6#######86	2	Perfect Duplicate
6#######37	2	Perfect Duplicate
Totals	21 women 46 entries	*Perfect Duplicate = 8* *Imperfect Duplicate = 4* *1 Admission, >1 Op = 4* *2 Admissions = 4* *Readmission = 2*

Figure 11. Flowchart of HES data preparation prior to Exeter batch search



No NHS Number

Of the remaining women who did not have a valid NHS number (N=286), home postcodes and date of birth were available for searching instead.

When NHS number and postcode were examined, a further duplicate record was identified which occurred three times. There were several instances of two women having the same date of birth and two instances of women having the same postcode, as one might anticipate, but only one perfect duplicate was present and as such was treated as the duplicate entries above. Thus there were N=284 women with a postcode and DOB combination, but without a NHS number.

Searching on NHS number and DOB had to be done individually but any records that were thus identified then had the NHS number added manually, to facilitate the third stage of data collection at the individual hospitals. Under the terms of PIAG approval, only new NHS number could be used at the hospitals - a form of ‘pseudoanonymisation’.

4.2 EXTRACTING STUDY DATA FROM 'OPEN EXETER'

4.2.1 Background and security

It was necessary for an honorary contract to be set up between the author and the West Midlands Cancer Intelligence Unit (WMCIU), and enhanced police clearance obtained as the data processed at the WMCIU is highly confidential. Appendix G includes details of these security measures.

A unique researcher ID and password were provided to enable access to the department computer network and to ensure generation of a clear audit trail. Additionally a separate, personalised log in and password were provided for use specifically with Open Exeter, authorised centrally as a further safeguard against fraudulent application or use.

The 'batch search' facility permitted searching of all ten local databases serving the West Midlands; hence the need for prior express permission from all ten data controllers for access to their data. If any had disagreed then the study could not have used this resource.

Theoretically, up-to 100 NHS number searches could be set to run concurrently. However, staff at WMCIU had previously established that, in practice, the system was laborious when more than 20 numbers were used in a batch search, so much so that that it became very slow and eventually 'crashed'.

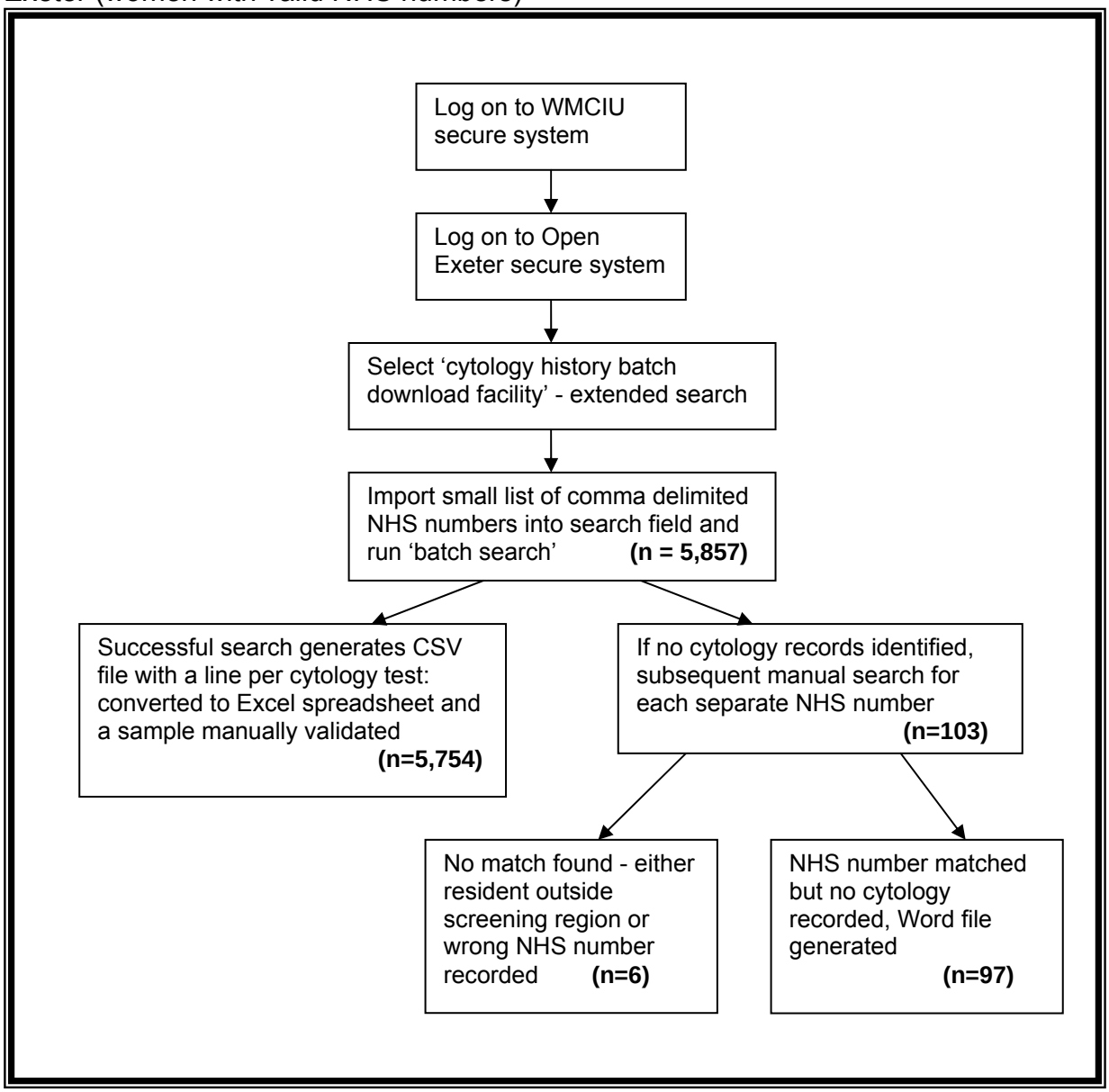
As data extraction for this study proceeded it became evident that, when optimum conditions were in place, 40 NHS numbers at a time could be searched on without precipitating processing problems. This data was immediately fed back to the data controller who implemented a policy change as a consequence.

4.2.2 Methodology of data extraction

Figure 12 is a flowchart which demonstrates the process steps necessary for searching using the batch download facility. It incorporates the numbers of records relating to each process step but is only applicable to women having valid modern NHS numbers; these did represent the great majority of study participants.

The output of each successful match was collated automatically into one file per batch search, which could be immediately viewed in Excel as a comma separated variable (CSV) file. Each was immediately converted into an Excel workbook containing all the relevant data, ready for collating and analysis. These workbooks included one line for every cytology test that the individual women had ever had (each duplicating all the demographic and registration data) so a search of 40 women could produce in excess of 200 lines of data as some women had over 20 results recorded. A standardised method of saving these small files was applied to ensure consistency and reproducibility.

Figure 12. Process steps for obtaining data using batch search facility in Open Exeter (women with valid NHS numbers)



For every batch of up to 40 records searched, manual validation was undertaken on at least one matched NHS number. The date of birth and postcode were compared with the date of birth and postcode from HES, thus manual double checking was undertaken on approximately 3% of the records. In all cases the match was perfect (100%).

When a batch search could not match a NHS number this was flagged up and later manually searched. Sometimes a manually input NHS number search would reveal the record to be present; in these cases the record was added to the database and the failure of the batch search noted to feedback to the data-controller.

In several cases the NHS number was known to the database but there was no record of a woman having ever had any cervical cytology tests; these women did not have any data to be output into Excel and so their demographic details had to be output to a Word file for collation later. These women, who had never had a smear test, were often noted to be older than the typical study population. This was not surprising; women born prior to 1/1/1923 were never routinely called to participate in the national cervical screening programme as they were already 'too old' when the programme was launched i.e. women over 84 years at the time of data extraction or over 81 years old during the year 2002-03 when the hysterectomies were undertaken. Additionally it is known that some women consistently decline the opportunity for cervical screening within the NHS for a wide range of reasons.[150]

Finally, a small number of NHS numbers could not be matched at all – there were several plausible reasons for this: the woman may be resident outside the region (having moved after her hysterectomy operation), the NHS number had been wrongly recorded in HES or that some inaccuracies were included in the cytology data. There was no way to establish which, if any, of these plausible explanations applied.

The 'batch search' use of NHS number meant that, of the HES database of 6,141 women, the 284 without a valid NHS number (4.6% of the total) could not be searched for this way. Thus individual manual searches of the relevant databases, using date of birth as the search variable with postcode then used for verification, was undertaken. Figure 13 summarises the process:

Figure 13. Process steps for obtaining data using batch search facility in Open Exeter (women without valid NHS numbers)

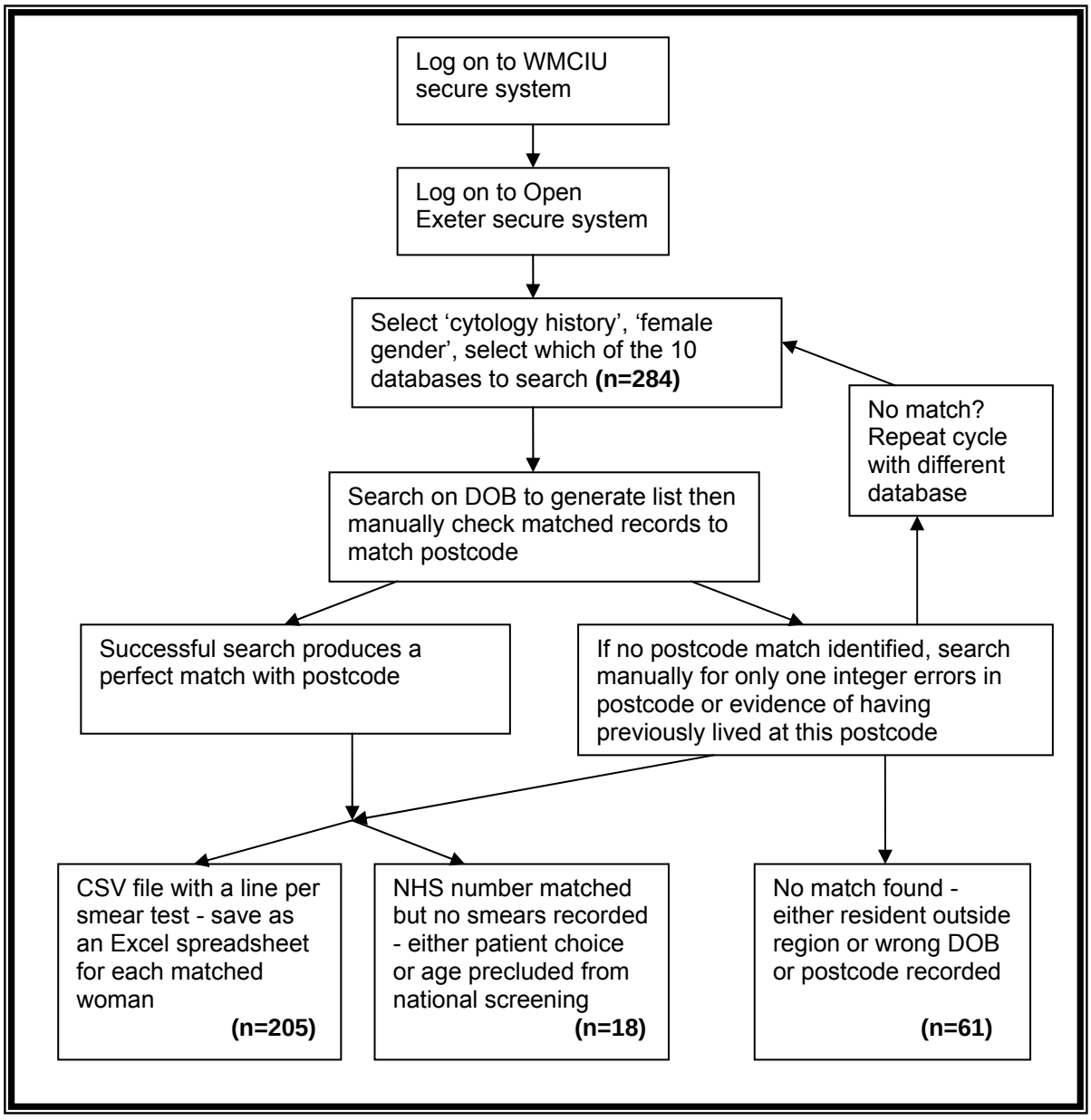


Table 15. Exeter data, format of the output Excel file

Name	Explanation
NHS number	New 10 digit
Name	Title Forename Surname (text string)
POS/DOUBT	Of uncertain significance, rarely used, historic field
Q code	PCT identifying code
Address	Full address as a text string, finishing with postcode
Date of birth	In the format dd/mm/yyyy
Age	In years, at date of data extraction (July 2007)
GP	GP name, address and postcode as a text string
GP Local Code	3 or 4 digit national code
#*	Smear number for that woman
Test date*	In the format dd.mm.yyyy
Reporting Lab	Text entry giving code or name of lab
Slide number*	Various types of numbering in use depending on lab, inconsistent
Result*	Numeric code - see separate table for description**
Infection*	A code added if suspicion of infection noted, see separate table for detail**
Action Code*	Cytology lab action code - numeric, see separate table for description**
Repeat Months*	Number of months until repeat smear advised - and recall set for
GP Local Code	Not always present - a numeric (up to 4 digit) code
Responsible PCSA	Name of PCT or Health Authority
Date Deducted	Date removed from recall
Reason for Movement	Reason for this removal from recall
Date of Death	Date Exeter has recorded for death of patient (not commonly used)
New PCSA Name	Of uncertain significance, rarely used, historic field
Recall date	Date that recall has been most recently set i.e. on the basis of most recent smear result
Notes*	Available for free text notes
Free Text	Second field available for free text or a spare column
Recall Type	Routine or Cancelled from further recall
Recall Status	No action / Cancelled / Non-respondent / GP informed
Notify Date*	Date of notification of no-respondent status or GP informed

** Unique data item to each record*

*** See Chapter 5.3, validation of Exeter data for relevant table*

4.2.3 Cytology history output

The entire cytology history for each participant was output into an Excel workbook and each line of the database contained the data summarised in Table 15. The table also highlights that some data is unique to each record (i.e. the details of that smear) but that for women having more than one smear ever, a significant amount of data was duplicated.

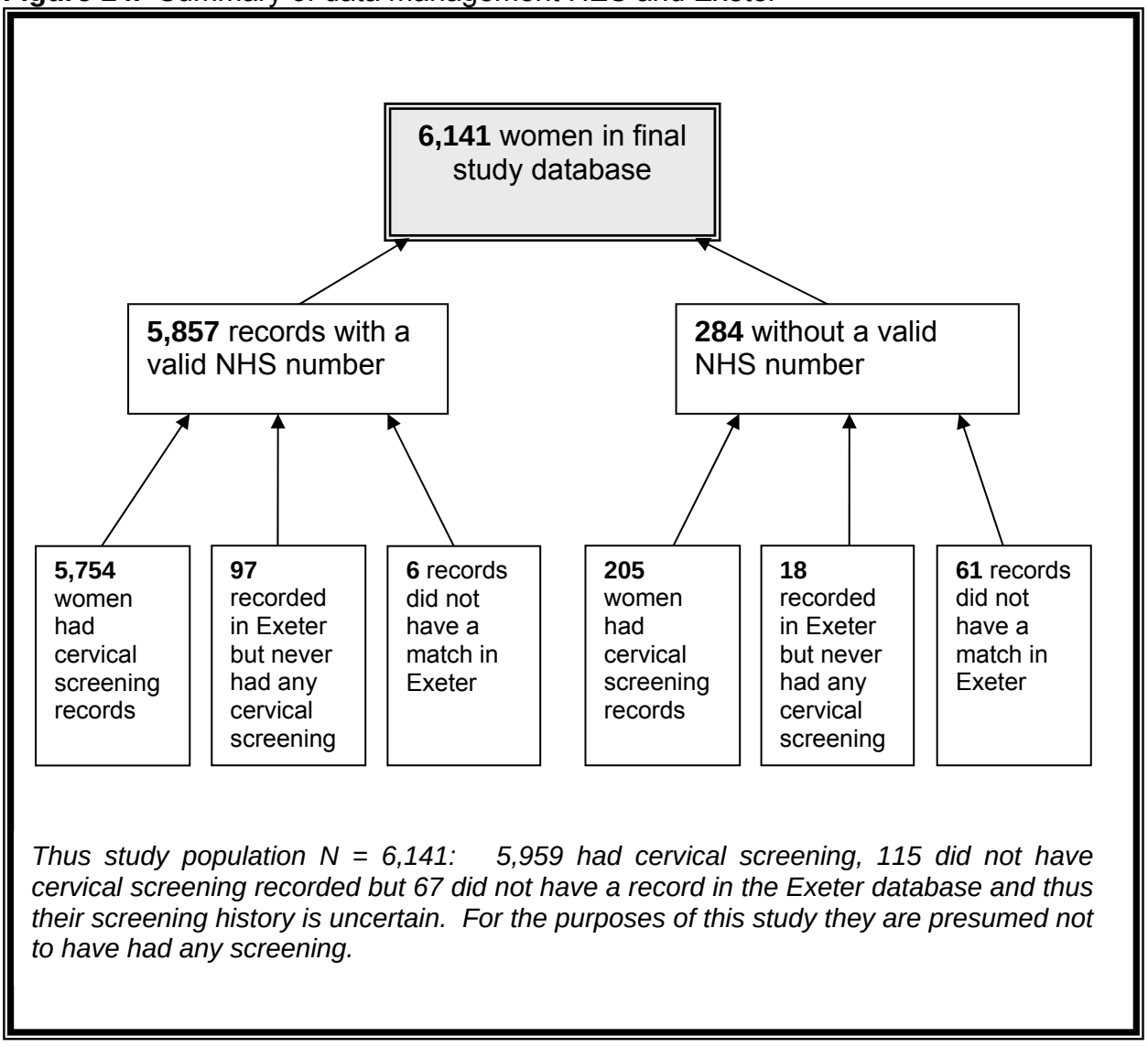
4.2.4 Managing the extracted data

The data, having been extracted into many small Excel files (N =171), required collation into one database thus the following data management stages were undertaken, summarised in Figure 14:

1. The 171 small Excel workbooks were merged to create one very large master workbook (5,754 NHS numbers).
2. Women without an NHS number, who had a perfect match or a one integer error in their postcode (current address or a previously recorded address) and perfect match of their date of birth, were appended to the main workbook (205 women), their NHS numbers were added from Exeter.
3. Records from all study participants who had never had a smear test were then manually transferred from Word into an Excel spreadsheet mirroring the main database, which was then appended to the main workbook (N= 115), their NHS numbers were also added from Exeter.

4. A small number of women could not be matched at all thus they had no records within the Exeter system (N=67). It was not possible to say whether or not they had ever had any cytology but for the purposes of the study it was assumed they had not.

Figure 14. Summary of data management HES and Exeter



The resulting Excel file included 36,649 lines of data on 6,074 (6141 - 67) women. Excel is able to handle approximately 65,000 lines of data in 256 columns for each line, but, if there are a lot of formulae containing cells included, this number is decreased.

The next step was to convert this long table of data, which included many lines of information for some women (one line representing every cytology test each woman had ever had), into a table containing only one line of data for each woman.

Excel was used to manage this process: data was sorted into NHS number order, those women never having any cytology had their missing values completed. Then the data was sorted into cytology test number order and then a formula applied 30 times to copy the cytology details from the rows below to the current row, thereby effectively 'moving up' the data. Figure 15 gives the formula used.

Figure 15. Generating one line of data for each study participant

To move cytology data from the next row of the spreadsheet up to spare cells on this row, only if the row below applies to the same person as this row:
Text: make this cell contain the same data as the cell specified if the cells both relate to the same NHS number, if not then insert a missing value code..
Code version = IF (A2=A#(?#,))*
*where # represents the relevant row number, ? the relevant column letter and * the relevant missing value 0 for date, 99 for result and 999 for number of months to repeat cytology advised)*

Due to the file size limitations of Excel this process had to be undertaken in batches and all the files collated. Once complete, all rows containing data on the first cytology test a woman had ever had, also contained her entire cytology record and thus these were extracted to create a new, complete database whereby each woman was represented by just one line of data.

4.3 MERGING THE DATASETS: FIRST STAGE, HES AND EXETER

Before merging of the HES and Exeter datasets could be undertaken, extensive data validation was necessary. This process is explained in some detail in Chapter 5; validation ensured that there were no unnecessary gaps in the data and avoidable errors could be identified and rectified to permit optimal matching.

In summary, the validated HES dataset contained 6,141 women of which all had valid dates of birth and postcodes and 6,055 had valid NHS numbers (98.9%). A decision was made to delete those fields which contained absolutely no data: DIAG 12/13/14, OPDATE 11/12. OPERTN11/12. All date fields were confirmed as such or converted into 'dates' in both Access and Excel and any missing discharge dates were calculated from duration of stay post operatively. Age at the day of surgery was calculated thus: (Operation date - Date of birth)/365.25.

The final, validated Exeter dataset included 6,065 records, of which, 6,064 had valid NHS numbers (the missing one matched HES on DOB and postcode perfectly). Postcode and date of birth were present in all 6,065. Empty columns and two containing free text were deleted: the 'Notes' column contained 88 entries, all relating to removal from recall but there was no standard format or information, the 'Free Text' column contained just 4 entries.

Given the very high percentage of records with an NHS number by the time of matching (Figure) and with the knowledge that NHS numbers had already been validated by HES, the first merge was simply done on the basis of this. Running a merge query in Access 2003® provided an identical match of 98.65% of the records first time; this is similar to levels achieved within the WMQARC.[151]

This preliminary data merging was an obligate step before coding of entire screening histories could take place (section 4.4) as date of hysterectomy had to be added to the cervical screening histories.

4.4 CLASSIFICATION OF LIFETIME SCREENING HISTORIES USING THE WEST MIDLANDS CANCER INTELLIGENCE UNIT QUALITY ASSURANCE REFERENCE CENTRE ALGORITHM.

4.4.1 Background and data preparation

It was important for the analysis of the final database to be able to classify and categorise the data in reproducible and standardised ways to allow for comparison with other populations. It was suggested that a pre-existing algorithm, recently developed by the West Midlands Cancer Intelligence Unit Quality Assurance Reference Centre (WMQARC) at Birmingham, for coding lifetime screening histories in women who developed cervical cancer, could be adopted for our purposes.[111]

This algorithm is fully reported in the Journal of Medical Screening, by Bagnall et al.[111] In essence, it is an Access® based visual basic programme which considers a woman's entire screening up until an 'event' date, in the case of the study the 'date of hysterectomy' and attempts to classify it in a logical, standardised, reproducible way. The syntax was generated 'in-house' at WMQARC and as such it was relatively straightforward to substitute the 'event date' from that of a cancer diagnosis to an operation date. However, it did mean that preliminary data matching was essential so that the date of hysterectomy could be included.

To be able to run the algorithm on the study data a specific format of cytology results was required and a set of assumptions about the population had to be made. These assumptions may be seen in full at Appendix H but, in summary, only women who have ever had screening at the appropriate age were included, tests taken in the private or in hospital sector were disregarded, apart from those near the recall date to ensure subsequent primary care follow-up is correct. Tests recommending referral were only included if they were taken at the 'usual' screening intervals; this was to assess how good the call-recall system was at detecting problems. Thus opportunistic testing, when a woman may present with other problems, was disregarded.

4.4.2 Running the algorithm

From a prepared Excel file containing a line for each screening test ever undergone by every woman in the study, the programme was run successfully. There were two outputs from the algorithm, provided in a simple Excel table with the patient identifiers DOB and new NHS number attached: The first was 'screening status'; a code indicating proximity of the last cytology test to the hysterectomy date, as outlined in Table 16. This measure was of uncertain relevance to the study as it assumed that the hysterectomy was related to the cervical cytology, however it was included for interest and possible analysis.

Table 16. Summary of Screening Status classifications

Classification	Meaning	#
I	Interval - hysterectomy occurred in between routine cytology testing	4,089
SD	Screen Detected - hysterectomy was within 6 months of a routine abnormal cytology test	62
SDD	Screen Detected Delayed - hysterectomy occurred more than 6months after an abnormal cytology test	115
LP	Lapsed - used to attend for screening but by time of hysterectomy was overdue	453
D	Defaulter - missed routine cytology tests despite reminders	190
DBI	Diagnosed Before Invitation - hysterectomy occurred before first invitation to routine cytology screening	2
NA	Non Attender - never attended for any cytology screening despite being eligible	101
NE	Never Eligible - above eligible age for screening via national programme	1,043
	Total	**6,055**

The second output was a 'summary code' for the entire Screening History, there are theoretically up to 4,320 of these five integer codes (6 x 5 x 6 x 6 x 4 integers). Figure 16 gives a few examples of this code to illustrate its complexity.

Each integer of the screening history code had a distinct meaning, these are explained further in Chapter 5.5.4.4. Essentially the process works through a flowchart, with 5 layers, each layer adding an integer to the code. Thus the coding is quite sophisticated. However, grouping of codes was possible to permit meaningful analysis.

Figure 16. Examples of Screening History codes

01113: Last cervical cytology test negative, taken less than six months before operation, but at some stage has had inadequate smears

10000: Never attended for a cervical cytology test despite being eligible and being called by the national programme

53112: Hysterectomy was undertaken at over 65 years of age, the last recorded cytology test was 5-10 years ago but she had all normal cytology tests throughout her screening history

4.4.3 Merging the algorithm data

The additional columns generated from running the algorithm could simply be added to the Excel version of the HES data as it mirrored it exactly. The NHS number and date of birth were added again but then removed after accurate merging of the columns to the HES database had been validated.

4.5 FINAL MERGING OF HES AND EXETER DATA, DEALING WITH DISCREPANCIES

Where NHS numbers were missing in HES, then Exeter had been searched for postcode and DOB matches. Perfect matches of both identifiers were accepted and automatically included. A small number of women with DOB matches had moved house some time between 2002/03 (when they had their surgery) and their most recent cytology test recorded in Exeter (up to June 2007), but one of their previous postcodes did match perfectly.

A small number of women, without an NHS number, had perfect DOB matches but had a postcode with an error in one integer. A decision was made to include these records as an imperfect match. No other imperfect matches were considered for inclusion. One record had no NHS number in either HES or Exeter but matched perfectly on DOB and Postcode and so a false NHS number of 9999999999 was allocated.

Once the algorithm data had been added to HES then the final merging of these datasets could take place. The merge query was run in Access 2003® then manual validation was undertaken on a random sample of 100 of the matched records. Random number tables were used to select row numbers and the author validated NHS number (100% accurate), date of birth (100% match) and postcode details.

There were several postcode discrepancies but when records were reviewed carefully this was either due to single digit transcription errors (an infrequent finding), or women had moved house following their hysterectomy and Exeter only searches on the most 'up to date' postcode for a woman. Table 17 summarises how data discrepancies were handled.

Then, for the small number of records in HES with the NHS number missing, date of birth and postcode were used to match the records using further merge queries. The merged data was turned into a new table using a 'make table' query in Access. This resulted in a table of 6,141 rows (each representing one woman) and 203 columns of data. 83 of these new records did not have any Exeter data included because there was no record of these women in the Exeter database. Throughout all these stages data was securely and frequently backed-up, in accordance with the study security protocol (Appendix D).

Finally, it was essential to apply a unique study identifier for each woman; had NHS numbers been universal in the HES data this could have been used even though it would have had to have been later removed at anonymisation. HES had already added its own unique number, the 'EPIKEY' to each admission, however, a small number of women had two EPIKEY numbers relating to more than one admission and so it was decided to add a completely new, unique study number which could be retained after anonymisation took place.

Table 17. Managing data discrepancies

Item	HES 6,141	Exeter 6,065	Algorithm 6,055	Notes for dealing with matching discrepancy
NHS number	6,067	6,064	6,055	The 6,067 in HES had all been verified to be true NHS numbers. The Exeter data set only contained one entry that did not have an NHS number. Those records in HES with no NHS number were supplemented with the NHS number from Exeter when this had been found. There were eventually 6 records with an NHS number from HES that could not be matched with an Exeter record, whereas there were 80 without NHS numbers that could not be found.
D.O.B.	6,141	6.065	6,055	Both HES and Exeter data were complete but the Exeter data was taken to be more reliable in case of conflict because a woman's normal cervical screening is undertaken on the basis of her age.
Postcode	6,141	6,064	Not included	HES data related to the hysterectomy operation whereas the Exeter postcodes related to the most recent recorded address (from July 2007) in their smear records so there were a few differences. The HES data was used because all these are validated (i.e. genuine) postcodes and relate to the time point of interest of the study.

4.6 HOSPITAL HISTOPATHOLOGY DATA

4.6.1 Obtaining hospitals data

To obtain data from the histopathology laboratories of the hospitals, PIAG stipulated that only the NHS number could be used as an identifier. Thus a simple data file was generated, from HES, of the study participants NHS numbers (where known) and the corresponding hospital where surgery had been undertaken. This file was taken to each of the chosen hospitals to obtain the data that they held concerning hysterectomy operations.

Three hospitals were all under the auspices of one NHS Foundation Trust by the data collection stage of the study. Thus a file was generated representing 829 women who were either recorded as having surgery in one of these hospitals or who lived within the postcode boundaries for routine care of those hospitals.

Hospital A

The intention had been to run a search on NHS number, at each of these trusts. However, at hospital A the laboratory manager advised that this would not be reliable as NHS number was not being used consistently in 2002-2003. A search was devised for all 'hysterectomy' specimens; it transpired that Hospital A was still using an outdated coding system for their samples – 'SNOP'. The Systemised Nomenclature of Pathology (SNOP) was a forerunner to the more widely used SNOMED codes (See Chapter 5.4 for further explanation).

The first search generated less than 140 records of hysterectomy specimens (Hospital A had over 400 according to HES) and so a wider search was undertaken of their entire database, this was subsequently interrogated for details of any gynaecological specimens generated during the required timeframe.

The resulting database initially included over 3,200 items; these contained duplicate records and single records spanning several lines thus giving the impression of being additional records. This data was then pseudoanonymised and cleansed to remove non-consultant samples, samples generated in the community, male patients (there were several) and samples taken in outpatient clinics. The final data set contained 923 lines of data and a merge query, in Access, found a perfect match for 383 of these women.

To validate this matching, a manual sample of 50 records was checked, unfortunately in 5 (10%) errors were found, usually where more than one sample was matched to a study patient, obviously only one could be the hysterectomy specimen. One had the SNOP code for an endometrial biopsy on a date prior to hysterectomy and the remaining 44 included many uterus specimen codes on the correct day but also codes for just cervix or just endometrium on the day of surgery. Thus the data was difficult to collate and did not seem to be standardised between patients. At an individual patient level however the laboratory could generate a comprehensive report of all specimens received.

Hospitals B and C

The same process had to be repeated at Hospital B, which had the histopathology data for Hospital C too. Although they use SNOMED coding there was confusion by staff as to which version was being used, and no key was available. There was also concern raised by staff that NHS number was 'not used reliably enough' to permit a valid search on the basis of this alone.

On this occasion, over 2,000 records were obtained. However the searches could not generate operation or sample dates on batch searching and so the output was of limited value as it was not possible to identify date order of samples and correlate these with operation dates. Additionally a lot of the data seemed incomplete with missing or incomplete morphology codes applied on 15% of the samples. As with hospital A, at an individual patient level it was possible to generate a comprehensive output of all histopathology reports and these included dates, however, these also included patient names and addresses and as such were not permissible for use in this study.

Hospital D

The process at Hospital D, a separate NHS Trust, was similarly troublesome with a search of their records for what the staff believed to be hysterectomy samples. This generated data on 214 women during the study period, whereas HES thought just 168 had a hysterectomy, of these the overlap was 127 women (75.5% of the HES cohort).

Decision making with respect to hospital level data

These hospital databases provided a powerful example of the limitations of routinely collected data. They functioned well for the requirements of the individual hospitals, having a comprehensive list of samples and sample identifying codes which permitted clinicians to access a separate 'hard copy register' of sample reports, for individual patients where there was no restriction on use of patient identifiers. However, for our purposes the data was of limited value.

Serious contemplation and study of the preliminary data that had been extracted was undertaken and several strategies attempted to increase the quality and matching potential. As some hospitals had refused access to their data and 814 study participants could not have their hospital identified, this level of data was never going to have been applied to all of the study population. However, it was frustrating to have access to data that was not suitable for matching.

After extracting data from just four hospitals the process was stopped as it was evident that there would be little to gain from persevering. The restrictions imposed by PIAG with respect to lack of patient identifiers proved to be the key limiting factor and a decision was reluctantly taken to not pursue this source of data.

4.6.2 Combining hospitals data with study database

The quality of the obtained hospitals data was variable and only applied to a small proportion of the study population, thus it was decided that it was more appropriate to keep this data separate rather than attempt to merge it with the main study data which was felt to be of high quality. The hospitals data was managed in Access, which permitted small subsets of data to be extracted and then converted to SPSS if necessary. No detailed statistical analysis could subsequently be undertaken on the hospitals' data.

4.7 ANONYMISING THE STUDY DATABASE

Once the final database of 6,141 women had been constructed and verified and the various key data items validated (see Chapter 5) then the three essential patient identifiers were removed i.e. date of birth, home postcode and new NHS number.

The secure removal of the identifiers was verified externally, as per study Security Policy (Appendix D) and PIAG was notified. Finally, the fully anonymised data could be transferred to a networked PC for analysis. All complex statistical analysis was performed in SPSS v 15.0, some of the descriptive work was undertaken in Excel 2003.

A back up copy of the database, including study identifiers prior to anonymisation was retained in a secure store (as per security protocol) for disaster management purposes only.

4.8 SUMMARY OF CHAPTER

This chapter has taken the reader through the many, necessary, steps in the process of obtaining data from the various datasets and highlighted some of the difficulties navigated. Using databases that were never designed for this style of interrogation highlighted some of their limitations whereas the bulk searching of NHS numbers in Exeter was an example of a good search facility that was seriously limited by a lack of computing power.

Despite efforts to use automated searching wherever possible it was inevitable that a small, but substantial, portion of data had to be searched for in more laborious ways. The ability to validate NHS number (See Appendix C) means that its use will inevitably increase; once NHS numbers are used universally through all NHS and related databases, these obstacles will disappear. Missing and duplicate records were dealt with systematically and the rules applied have been justified.

Several conversions of the various types of data had to take place from text files to Excel spreadsheets and then to Access relational databases. Both these computing applications were used for different stages of the extraction and linkage: Excel was particularly helpful for converting long lists of cervical screening test results to one line of data per study participant. Access, with its ability to run 'merge' and 'make-table' queries was invaluable for linking the datasets, without the need for writing a bespoke computer program.

The final merged database, from HES and Exeter, was of high quality and populated with a wide range of data on each study participant's hospital stay, operation type and outcome, her entire cervical screening history and a coding of this. However, the data obtained from hospital histopathology laboratories was very disappointing and, after efforts to improve the quality failed, this resource was no longer pursued. Full anonymisation of the study database was confirmed and analysis could then begin.

CHAPTER FIVE: DATA VALIDATION AND CODING

INTRODUCTION TO CHAPTER

The chapter deals with the preliminary management of the various items of data, once they had been successfully extracted from their respective sources. This management and subsequent manipulation was necessary to ensure the data were free from errors and duplication; a vital process step before merging the data sets to maximise matching and ensure that numbers of mismatched items would be minimised

The sets of data are considered in the order they were obtained i.e. HES data concerning the hospital admission for hysterectomy, 'Exeter' data concerning women's entire cervical screening histories and finally the hospital laboratory data .

Once the final dataset had been created and anonymised (as has already been outlined in Chapter 4) it was necessary to classify and code some data to allow for meaningful comparisons and statistical analysis; coding is described towards the end of the chapter.

5.1 VALIDATION METHODS

Data validation tests are generally applied to ensure that data conforms to specific rules. In data collection systems, where the researcher has control over the raw data, simple validation rules can be applied to inputting forms to ensure that data is in the correct format or that entered values are plausible (i.e. not accepting dates of birth prior to 1st January 1899). However, when using routinely collected datasets, the researcher does not have initial ownership of the data inputting stage and so validation of routinely collated data is essential to confirm that all data items are genuine, accurate and contain no obvious errors.[109;152]

Phases of data validation often include:

1. Missing values: These may be a single integer missing or a whole entry skipped. It is important to quantify these and then to standardise them into different types i.e. whether missing through human error or if this is genuinely unknown information. It may be important to know this distinction during subsequent data coding. It may be possible to 'fill in the gaps' especially where data has been duplicated (i.e. in the case of a repeated test) or where another data source can be accessed.

2. Invalid data: This may take many forms; it may represent the wrong number of characters (i.e. in a postcode), impossible values (i.e. age >115, or 'hysterectomy operation' in a male) or simple typographical error (i.e. test type recorded as 'valt' instead of 'vault'). Some may have to be excluded from analysis; other items may be amenable to correction.

3. Consistent data: Checking for consistency may be helpful to confirm if data has been transferred effectively: if there are particularly unexpected findings i.e. no births in a particular year or no operations performed in one hospital in a given month. This acts as an 'alert' that a problem may have occurred at some stage and the data requires closer scrutiny. Further investigation may reveal operator errors or programming errors in data linkage.

These three main approaches were applied to all the received study data and are outlined below, with specific mention being made of instances where there were problems identified with the data.

5.2 HES DATA VALIDATION

The requested data extract was received from Northgate Information Solutions on a CD-Rom containing a text file of two data sets, in pipe delimited style (see Chapter 4.1 for explanation), which was converted to Excel for preliminary validation.

5.2.1 Summary of all the received data

Table 18 summarises all the different received 'fields' or headings in the main data file from HES, the number of included records for each and the degree to which the data was complete and valid. Records with 100% valid entries are in bold type.

It may be seen that postcode and date of birth were present in 100% of cases but new NHS number was present for 95.4%. The names of fields used were those supplied by HES and are compatible with all HES outputs. There is a brief explanation of each in the table, however, further explanation may be found in then next section.

Table 18: Summary table of all the received HES data items

No.	Code	What the code is for	Valid	Incomplete or invalid	Missing or not recorded
1	DOB	Date of birth (date field)	**6,168**	0	0
2	ETHNOS	Ethnic Group of patient	4,226	1,942	0
3	NEWNHSNO	New NHS Number	5,882	1	285
4	SEX	Gender (all female)	**6,168**	0	0
5	ADMIDATE	Date of admission to hospital (date)	**6,168**	0	0
6	DISDATE	Date of discharge from hospital (date)	6,120	42	0
7	DISDEST	Discharged destination	6,120	47	1
8	MAINSPEF	Speciality of consultant	**6,168**	0	0
9	TRETSPEF	Treatment speciality of consultant	**6,168**	0	0
10	**EPITYPE**	Type of admission	**6,168**	0	0
11	DIAG01	Diagnosis code: up to 14 per admission for each woman ICD10 codes	**6,168**	0	0
12	DIAG02		6,163	0	5
13	DIAG03		1,325	0	4,843
14	DIAG04		518	0	5,650
15	DIAG05		197	0	5,971
16	DIAG06		84	0	6,084
17	DIAG07		31	0	6,137
18	DIAG08		10	0	6,158
19	DIAG09		4	0	6,164
20	DIAG10		2	0	6,166
21	DIAG11		1	0	6,167
22	DIAG12 *		0	0	6,168
23	DIAG13 *		0	0	6,168
24	DIAG14 *		0	0	6,168
25	OPDATE01	Date of operation: up to 12 dates per episode for each woman	6,163	5	0
26	OPDATE02		4,965	31	1,172
27	OPDATE03		1,814	15	4,339
28	OPDATE04		638	7	5,523
29	OPDATE05		157	0	6,011
30	OPDATE06		50	0	6,118
31	OPDATE07		18	0	6,150
32	OPDATE08		6	0	6,162
33	OPDATE09		3	0	6,165

34	OPDATE10		1	0	6,167
35	OPDATE11 *		0	0	6,168
36	OPDATE12 *		0	0	6,168
37	OPERSTAT	Was operation carried out or not	5,736	429	3
38	OPERTN01	Operation code: OPCS4 (Classification of Surgical Operations and Procedures) codes with the full-stop, that is usually located between the 2nd and 3rd digits, omitted OPERTN01 should represent the main operation that was carried out	**6,168**	0	0
39	OPERTN02		4,998	0	1,163
40	OPERTN03		1,829	1	4,338
41	OPERTN04		645	0	5,516
42	OPERTN05		157	0	6,011
43	OPERTN06		50	0	6,118
44	OPERTN07		18	0	6,150
45	OPERTN08		6	0	6,162
46	OPERTN09		3	0	6,165
47	OPERTN10		1	0	6,167
48	OPERTN11 *		0	0	6,168
49	OPERTN12 *		0	0	6,168
50	POSOPDUR	Days in hospital after main surgery	6,163	0	5
51	SITETRET	Hospital where operation conducted	5,354	102	712
52	OACODE	Super Output area (SOA) of residence	**6,168**	0	0
53	OACODE6	6-character SOA of residence	**6,168**	0	0
54	WARD91	Electoral ward of residence	6,128	40	0
55	RESPCT	PCT of residence	**6,168**	0	0
56	HOMEADD	Patients home postcode	**6,168**	0	0
57	PCTTREAT	PCT where treatment occurred	**6,168**	0	0
58	ROTREAT	Region where treatment occurred	**6,168**	0	0
59	STHATRET	Strategic HA where treatment occurred	**6,168**	0	0
60	CONSULT	GMC number identifying consultants	6,167	1	0
61	GPPRAC	General Practitioner surgeries code	6,157	11	0
62	EPIKEY	A record identifier (unique) created by HES	**6,168**	0	0

** Seven fields contained no data at all and thus were omitted from further analysis.*

5.2.2 Expanded validation data on some fields

DOB = Date of birth: This was a complete data set, which was important to the study as this was one of the three linkage items. Of interest, 10 women were aged over 90 at the time of their surgery (i.e. DOB prior to 1912) and two women were aged under the age of 20 at the time of surgery (i.e. DOB after 1982). No dates of birth were implausible and thus this field was taken to be completely accurate and used as the basis for all subsequent age related calculations.

ETHNOS = Ethnic Group of patient: From 2001 HES ethnicity codes were changed to conform to the 2001 census classification. Unfortunately ethnicity was recorded somewhat erratically during 2002-2003 and only 68.5% of women had this recorded. The great majority of women were White British (86.4%) but there was representation from every ethnic grouping amongst the study population. Table 19 has a summary of all supplied ethnicity data.

DISDEST - **Discharged from hospital destination**: This field gave information about the place that patient intended to go to on leaving hospital. Table 20 summarises the validation of this field, it may be seen that ten patients were recorded as having died during the admission but 47 (0.76%) had discharge information missing. The great majority were discharged to their usual place of residence.

Table 19: Summary of supplied ethnicity data

HES Code	Meaning	Code for analysis	N	% (6,168)	% of coded women (4,226)
A	British (White)	0	3,653	58.9	86.4
B	Irish (White)	1	28	0.5	0.7
C	Any other White background	2	174	2.8	4.1
D	White & Black Caribbean (mixed)	3	12	0.2	0.3
E	White and Black African (mixed)	4	1	0.0	0.0
F	White & Asian (mixed)	5	1	0.0	0.0
G	Any other Mixed background	6	1	0.0	0.0
H	Indian (Asian or Asian British)	7	120	1.9	2.8
J	Pakistani (Asian or Asian British)	8	72	1.2	1.7
K	Bangladeshi (Asian or Asian British)	10	7	0.1	0.2
L	Any other Asian background	11	10	0.2	0.2
M	Caribbean (Black or Black British)	12	91	1.5	2.2
N	African (Black or Black British)	13	15	0.2	0.4
P	Any other Black background	14	13	0.2	3.1
R	Chinese (other ethnic group)	15	11	0.2	0.3
S	Any other ethnic group	16	17	0.3	0.4
	Subtotal of classified ethnic group		*4,226*	*68.5*	***100***
X	(not a genuine code)	99	26	4.2	
Z	Not stated / missing		1,165	18.9	
0	(not a genuine code)		635	10.3	
1	(not a genuine code)		22	0.4	
2	(not a genuine code)		3	0.0	
9	(not a genuine code)		91	1.5	
	Subtotal of unclassified ethnic group		*1,942*	*31.5*	
Total			***6,168***	***100***	

Table 20: Summary of destination information

Value	**Meanings of codes** (all possible)	Number	%
19	Usual place of residence (incl. no fixed abode) = home	6,048	98.05
29	Temporary place of residence (i.e. hotels, schools)	25	4.05
38	Penal establishment - police station	1	0.02
49	NHS other hospital provider - high security psychiatric unit	1	0.02
51	NHS other hospital provider - ward for general patients or younger physically disabled.	18	2.92
52	NHS other hospital provider - ward for maternity patients or neonates	1	0.02
54	NHS run nursing home, residential care home or group home	3	0.05
65	Local Authority Part 3 residential accommodation - where care is provided	11	0.18
79	Patient died	**10**	0.16
84-89	Non NHS institutions	2	0.03
98	Not applicable	47	0.76
39	*not a genuine code*	*1*	*0.02*
Total		***6,168***	***100***

MAINSPEF = Speciality of consultant, the medical speciality that the consultant is contracted under, during period of care and **TRETSPEF = Treatment speciality of consultant** during period of care: these two fields would usually be the same. Table 21 indicates that there were only a few minor differences between the groups, with the vast majority of cases being under the care of gynaecologists or obstetricians.

Table 21: Summary of MAINSPEF and TREATSPEF validation

Code	Meaning	Number MAINSPEF	%	Number TRETSPEF	%
100	General surgery	64	*1.04*	63	*1.02*
101	Urology	13	*0.21*	13	*0.21*
300	General Medicine	6	*0.10*	2	*0.03*
370	Medical oncology	1	*0.02*	1	*0.02*
501	Obstetrics	25	*0.39*	24	*0.39*
502	Gynaecology	6,058	*98.22*	5,745	*93.14*
&	TREFSPEF = MAINSPEF			320	*5.19*
800	Clinical oncology (Radiotherapy)	1	*0.02*	0	*0*
Total		***6,168***	***100***	***6,168***	***100***

EPITYPE = Type of inpatient episode: This was useful to identify those women who underwent an emergency hysterectomy during or just after childbirth, the data was complete with only 25 women being coded as having had a 'delivery' episode and is consistent with 25 women being under the care of an Obstetrician (Table 21).

DIAG = ICD10 diagnosis codes:[139] These codes were crucial to permit coding women for analysis on the basis of their diagnosis. Although up to 14 are permissible in HES, the majority of women had just two codes, see Section 3.2.2.1 for further detail about ICD10.

OPDATE = Operation date: dates of all procedures undertaken whilst an in-patient. This permitted duration of hospital stay to be calculated.

OPERSTAT = Operation status code: this confirmed that a surgical procedure was carried out. Of interest, 428 women had a code suggesting that no operation occurred (Table 22), but all of these had documented operation codes. There were no invalid codes and only one entry was missing but in view of the large number of obviously erroneous entries this field was not used further.

Table 22: Operative status: Did surgery take place?

Value	Meaning	Number
1	One or more operation carried out	5,736
8	Not applicable - no operation carried out	428
9	Not known - no data entered	1
-	Missing data	3

OPERTN = Operation code: These fields are the OPCS4 (UK Classification of Surgical Operations and Procedures) codes,[153] however the usual full-stop between the 2nd and 3rd digits in this code had been omitted by HES. Chapter 3.2.2.2 has already outlined the structure and content of OPCS4 codes.[126] OPERTN01 in HES is intended to represent the 'main' operative procedure that was undertaken and all 6,168 records included a valid code in this field. All the codes included in the other fields were found to be valid (Table 18). In total, HES had 13,875 OPCS4 codes documented for these 6,168 cases.

POSOPDUR = Post operative duration of stay: The number of days from the date of operation to date of discharge from that hospital, these were whole or part days recorded in all but 5 cases. However, those five cases did have dates for hospital discharge and operation dates so this field was calculated and input manually. Of concern, however, was that 114 records suggested that women were discharged on the day of surgery (see Table 23) and seven women were in hospital for 40 days or more. Whilst the longer duration of hospital stay is plausible if a woman experienced surgical complications or had severe disease, to be discharged home following major surgery, within 24 hours, seems highly improbable and would suggest miscoding of either the operation or the discharge date/destination.

SITETRET = Site of the treatment: a code for the individual hospitals where surgery had occurred, thus, more specific than just coding the relevant NHS Trust. Hospitals are only identified by a code in this thesis, to preserve confidentiality of both patients and clinicians. Table 24 summarises these data and illustrates several problems that were identified: Firstly, three hospitals within the region, which definitely have gynaecology departments and at which hysterectomy operations are known to occur, did not have any operations recorded for the study period. However, there were 712 instances of missing or just one-digit codes being applied and this coincides closely with the approximate number of cases that would have been anticipated as being undertaken at these three sites. Crude postcode data supported the hypothesis that cases from these particular hospitals may have just had this coding omitted but a decision was made not to 'assign' women to a given hospital but to work with and analyse just the supplied hospitals data.

Table 23: Duration of hospital stay, post operatively

No days	N	Collated	No days	N	Collated
Missing	5	5	*20*	4	
0	114	114	*21*	6	
1	40	125	*22*	4	
2	85		*23*	5	
3	872		*24*	2	34
4	1,936	**5,049**	*25*	2	
5	1,605		*26*	2	
6	636		*27*	3	
7	335		*28*	4	
8	184	662	*29*	2	
9	90		*31*	3	
10	53		*32*	1	6
11	44		*34*	1	
12	33		*38*	1	
13	18		*40*	1	
14	23		*42*	1	
15	15	166	*47*	2	
16	10		*50*	1	7
17	6		*51*	1	
18	10		*81*	1	
19	7				

A major University Hospital NHS Trust in the West Midlands has no department of gynaecology or obstetrics on site at either of its two hospitals (these being located at a nearby women's hospital), however, a small number of operations (18) were performed here and these may represent cases of emergency surgery or a hysterectomy being undertaken as part of more major bowel surgery.

Table 24: Hospital at which hysterectomy was performed

Hospital Code	No samples	% total N=6,168
1	245	3.97
2	167	2.71
3	216	3.50
4	408	6.61
5	169	2.74
6	375	6.08
7	413	6.70
8	649	10.52
University Hospital, no gynaecology on site	18	0.29
9	366	5.93
10	414	6.71
Odd finding as Gynaecology on site	0	0
11	224	3.63
12	274	4.44
13	352	5.71
14	157	2.55
15	368	5.97
Maternity hospital only, same trust as 16	6	6.78
16	412	
Odd finding as Gynaecology on site	0	0
Total of cases within the region	**5,215**	**84.55**
Out of area 10 hospitals	121	1.96
Code does not exist	84	1.36
Private provider / incomplete	18	0.29
Missing data or one digit only	712	11.54
Total incomplete or outside region	**935**	**15.45**

121 operations were coded as being conducted out of the region; the great majority (113) were hospitals that border the West Midlands (i.e. Gloucester, Oxford, Derby and East Cheshire) and may represent cases referred to tertiary centres or an expression of patient choice. For those recorded as being significantly outside the region it is possible that women had relocated but their hospital records had not been updated or that emergency surgery was undertaken during a vacation.

OACODE / OACODE(6) = Census output area: This code was applied by HES and was based on the home postcode of the patient and thus is a derived field. Both the full (10 integer) and restricted (six integer) codes are supplied. Output Areas (OAs) are small geographical areas that cover similar population sizes, according to the 2001 census and are as socially homogeneous as possible.[154] There are 165,665 OAs in England. The six character version includes three two-letter codes combined i.e. CCDDWW (CC = county, DD = district, WW=ward).

RESPCT = Patients Primary Care Trust of residence: This is another HES derived code, by applying patient postcode of usual residence. All these codes start with five then two letters representing the various PCTs (Table 25). Some of these subsequently changed in 2006.

HOMEADD = Full UK Postcode: Postcode of patient's recorded home address, using the eight alphanumeric style, where spaces are used to 'pad out' shorter postcodes.[123] Table 26 summarises the various regions, it may be seen that 20 women lived outside the traditional West Midlands boundary (designated with a *).

Table 25: PCT Codes and numbers of study participants

Code	PCT Name	N	Code	PCT Name	N
5CN	Herefordshire	185	5MG	Oldbury and Smethwick	93
5D1	Solihull	192	5MH	Rowley Regis and Tipton	129
5DQ	Burntwood, Lichfield and Tamworth	208	5MJ	Wednesbury and West Bromwich	153
5DT	North East Oxfordshire	110	5MK	Telford and Wrekin	188
5HR	Staffordshire Moorlands	119	5ML	East Staffordshire	139
5HT	Dudley South	224	5MM	Cannock Chase	231
5HV	Dudley Beacon and Castle	145	5MN	South Western Staffordshire	260
5HW	Newcastle-under-Lyme	104	5MP	North Warwickshire	287
5M1	South Birmingham	499	5MQ	South Warwickshire	269
5M2	Shropshire County	292	5MR	Redditch and Bromsgrove	193
5M3	Walsall Teaching	366	5MT	South Worcestershire	302
5M9	Rugby	84	5MV	Wolverhampton City	211
5MD	Coventry Teaching	315	5MW	North Birmingham	186
5ME	North Stoke	119	5MX	Heart of Birmingham	213
5MF	South Stoke	102	5MY	Eastern Birmingham	250
Totals					***6,168***

Table 26: West Midlands postcode regions and numbers of study participants[123]

Postcode	Location	Number	Postcode	Location	Number (N)
B	Birmingham	2,087	*OX**	*Oxford*	*7*
CV	Coventry	872	*SK**	*Stockport*	*3*
*CW**	*Crewe*	*7*	ST	Stoke	654
DE	Derby	108	SY	Shrewsbury	218
DY	Dudley	482	TF	Telford	237
GL	Gloucester	7	WR	Worcester	294
HR	Hereford	173	WS	Walsall / Lichfield	661
*LE**	*Leicester*	*3*	WV	Wolverhampton	355
Totals					***6,168***

** Italics represent postcodes outside the West Midlands region.*

PCTTREAT = Primary Care Trust of treatment: A derived code based on the hospital providing surgery. All codes start with '5' then two letters representing the local Primary Care Trusts (PCT) as summarised in Table 27.

ROTREAT = Region of treatment: A field recording geographical location of treatment; this was a main regional classification, summarised in Table 28.

STHTRET = Strategic Health Authority (SHA) of treatment. Summarised in Table 29, a small number of SHAs were geographically remote from the West Midlands.

CONSULT = The GMC Code (number): This identifies the responsible consultant individually. There was only one code for a missing data item, the rest were valid GMC codes.[143] These have not been summarised but there were 6167 valid codes representing 233 different doctors.

GPPRAC = Registered GP Practice of patient: This code allows the practice to be notified about any treatment administered. However the registered GP may not be the same as the referring GP. 6,157 women had valid GP practice codes, two were registered with Ministry of Defence (MoD) doctors and nine did not have this data recorded.

Table 27: Primary Care Trust of treatment

Code	PCT Name	N	Notes
5AA	South Manchester	2	*out of area*
5AL	Central Derby	15	*out of area*
5CL	Central Manchester	1	*out of area*
5CN	Herefordshire	167	
5DD	Morecombe Bay**	1	*out of area*
5DW	Oxford City	20	*out of area*
5EJ	Leicester City West	5	*out of area*
5F5	Salford	1	*out of area*
5F7	Stockport	2	*out of area*
5FA	Ashfield**	1	*significantly out of area*
5H1	Hammersmith and Fulham**	1	*significantly out of area*
5H4	Central Cheshire	3	*out of area*
5H5	Eastern Cheshire	33	*out of area*
5HT	Dudley South	367	
5K3	Swindon**	2	*significantly out of area*
5KT	Central Cornwall**	1	*significantly out of area*
5KW	Cheltenham and Tewkesbury	51	*out of area*
5M1	South Birmingham	667	
5M2	Shropshire County	434	
5M3	Walsall Teaching	352	
5MD	Coventry Teaching	408	
5MF	South Stoke	418	
5ML	East Staffordshire	157	
5MN	South Western Staffordshire	384	
5MP	North Warwickshire	269	
5MQ	South Warwickshire	215	
5MT	South Worcestershire	544	
5MV	Wolverhampton City	301	
5MW	North Birmingham	434	
5MX	Heart of Birmingham	911	
5C6	*Invalid code*	*1*	*only one miscoded entry*
Totals		***6,168***	

Table 28: Region of treatment

Code	Region	Number
Y02	Trent	20
Y07	**West Midlands**	**6,030**
Y08	North West	42
Y10	London	2
Y11	South East	20
Y12	South West	54
Total		***6,168***

Table 29: Strategic Health Authority of treatment

Code	Strategic Health Authority	N
Q04	North West London	1
Q06	North East London	1
Q13	Cumbria and Lancashire	1
Q14	Greater Manchester	6
Q15	Cheshire & Merseyside	36
Q16	Thames Valley	20
Q20	Avon, Gloucestershire and Wiltshire	53
Q21	South West Peninsula	1
Q24	Trent	16
Q25	Leicestershire, Northamptonshire and Rutland	5
Q26	**Shropshire and Staffordshire**	**1,393**
Q27	**Birmingham and the Black Country**	**3,031**
Q28	**Coventry, Warwickshire, Herefordshire, Worcestershire**	**1,604**
Total		***6,168***

Thus, overall the HES data was comprehensive and valid with the few notable exceptions of relevance to this study being ethnicity and hospital of treatment.

5.3 EXETER DATA

Chapter 4 has already outlined the processes involved in extracting and combining all the Exeter data into one large spreadsheet of 6,065 women, created from the 36,469 lines of cytology results data.

Validating this new database was less complex than the validation required for HES data as there were fewer variables and Exeter has some inbuilt validation i.e. as age is the trigger that sets call and recall to the various national screening programmes then date of birth is a mandatory field. NHS number is also a pre-requisite, thus it is difficult to add any data to Exeter files without having a valid NHS number.

When a woman had undergone at least one cytology screening test in her lifetime the 'Exeter' database held all the data items, summarised within Table 30, for each separate test. Thus, theoretically, a single woman could have over thirty records if she had ever had any abnormal tests with early recall recommended.

Currently, in England, a woman who only has negative cytology tests would usually have a maximum of 11 tests in her lifetime,[83] however guidelines have changed over the years since the screening programme started and have varied around the UK and so some women could, theoretically have had up to 15 consecutive normal cytology test results (three yearly from 20 - 65 years).

Table 30 also shows which items were unique and which were duplicated on all tests recorded for a given woman. Some completely irrelevant data items have not been included and some of those items included were subsequently discarded from the database prior to analysis (indicated by 'R').

A few of these data items warrant further explanation: Table 31 includes details of all possible cytology results codes, subsequent recommended action and details of those codes representing any infection detected. Every test should have had a result code and an action code documented, but infection codes were only applied if relevant with the default being a blank cell representing 'no infection detected'.

Thus, it may be seen from Table 31, that the overall cytology results gave an inadequate specimen rate of 6.31%, borderline results represented 4.05% with the likelihood of a normal (negative) result being 85%. Infection was uncommon, with only 3.07% of tests having an infection code added; candida (fungal) infection was most prevalent, being noted in 1.77% of all tests.

Address and postcode

The Exeter system does not hold postcode as a separate field, thus to establish the patient's postcode from the address string it was necessary to use special functions in Excel: the address 'string' took the form of one line with commas separating the address items thus the string was split using the 'Text to Columns' function, with the comma as the separating variable. Then the postcode column could be extracted, ready for use in linkage and to apply a deprivation classification.

Table 30: Exeter data items for each recorded cytology test

Title	Notes	Unique = U Duplicated = D Irrelevant = R	Number of items* (N=6,065)	%
NHS number	New 10 digit	D	6,064	99.98
Name	Title Forename Surname (string)	D	6,065	100
Q code	PCT Code	D	6,053	99.80
Address	Full address (string) inc postcode	D	6,060	99.92
Date of birth	'dd/mm/yyyy' format	D	6,065	100
Age	In years, at time of data extraction	D	6,065	100
GP	GP name, address, postcode (string)	D	6,054	99.82
GP Local Code	3 or 4 digit, (string)	D	6,015	99.18
#	Smear number	D	6,065	100
Test date	'dd.mm.yyyy' format	U	5,810	5,810
Reporting Lab	Text field	U	-	-
Slide number	Various formats, depending on hospital processing the test	U	-	-
Result	Numeric code - see later for description	U	5,810	95.80
Infection	A coded added if suspicion of infection noted	U	174	2.87
Action Code	Cytology lab action code - numeric, see separate table for description	U	5,810	95.80
Repeat Months	Number of months until repeat smear advised	U	4,433	73.09
GP Local Code	Numeric (up to 4-digit) code	D	6,065	100
Date Deducted	Date removed from recall	R	59	0.97
Reason for Movement	Reason for this removal from recall	U	59	0.97
Date of Death	Date Exeter has for death of patient	U	343	5.66
Recall date	Date for recall on the basis of most recent smear result	U	5,594	98.17
Notes	Option for free text (string)	U	-	-
Recall Type	Routine or Cancelled from further recall	U	5,594	98.17
Recall Status	No action / Cancelled / Non-respondent / GP informed	D	5,594	98.17
Notify Date	Date of notification of no-respondent status or GP informed	R	-	-

* *The 'number of items' field refers to the database of 6,065 women. Demographic data related to the most recent screening test, however, the result related to the first recorded cytology test only.*

Table 31: Explanation of data items in cytology extract

Details of cytology 'Results Codes'		
Results Code	**Interpretation**	**N = 36,213**
1	Inadequate Specimen	2,284
2	Negative	30,772
3	Mild Dyskaryosis (CIN 1)	851
4	Severe Dyskaryosis (CIN 3)	411
5	Severe Dyskaryosis / Possible Invasive Carcinoma	48
6	Possible Glandular Neoplasia	87
7	Moderate Dyskaryosis (CIN 2)	295
8 / B	Borderline	1,465

Details of cytology 'Action Codes'		
Action Code	**Description**	**N = 36,213**
A	To be used for all cases where the next test is to be performed at the normal (routine) recall interval for the health authority responsible for the women	25,882
R	To be used for all cases in which a further smear is recommended in an interval less than the routine recall interval of the DHA	8,110
S	To be used for all cases where a referral to a gynaecologist is recommended and for those smears from patients under the care of a gynaecologist or other relevant specialist	2,211
H	Record the result and do not change current recall details	10

Cytology infection code descriptions		
Code	**Description**	**N = 1,113**
1	Trichomonas present	52
2	Candida present	640
3	Wart virus present	248
5	Actinomyces present	44
6 / 7	Other infection (to be specified) present	129

Dates

To convert dates from non-standard formats from Exeter to standard formats for analysis the “Text to Columns” function in Excel was applied with ‘delimiting’ left blank and the ‘DMY’ option selected. This process was used for every date field to ensure that date fields were compatible.

Overall the quality of the cervical screening data obtained from the QARC was excellent; the data was comprehensive and contemporaneous and of better quality than had been anticipated.

5.4 HOSPITALS' DATA

The hospitals in the study area used a variety of software programmes to store and archive their histopathology data. Three NHS trusts, representing four distinct hospitals were selected for use at this stage of the project, representing a diverse range of affluence and population density: Hospital A located in an affluent suburb of Birmingham (hospital 10 in Table 24 and Chapter 6). Hospital B located in a more densely populated urban setting also included data from Hospital C which is part of the same NHS Trust and located in another affluent suburb (combined as hospital 7 in Table 24). Finally, Hospital D, located in a small town centre, covered a largely rural population (hospital 2 in Table 24).

A wide range of variety of computer programmes are used by hospital pathology laboratories to manage their patient records ranging from bespoke programmes developed locally 20 years ago through to Windows based spreadsheets or relational databases. Table 32 summarises the data held at each of these sites that was made available to this study.

The Systematized Nomenclature of Pathology (SNOP) was developed in the 1960s by the College of American Pathologists (CAP) and American Cancer Society (ACS) as a coding system for pathological specimens.[142] There were two groups of codes, the Morphology or M codes to describe form and structure of the specimen (the diagnosis) with the Typography or T codes used to describe the anatomical region or body part that the sample came from.

The pathology laboratory at Hospital A had retained SNOP coding from the 1970s and never transferred their records over to the newer SNOMED system. The recent merger with the NHS Trust of hospitals B and C meant that at the time of data extraction the transfer was being planned. This use of an old coding scheme produced difficulties with respect to aggregating data; conversion algorithms were being developed at the time, but these were not yet ready for use.

Table 32 includes a summary of the data that were extracted from the hospitals including the numbers of records compared with the numbers of HES cases, the proportion of records including NHS number and some notes.

All the laboratories were confident that their own systems would allow a clinician to access reports, for a named patient, to determine the diagnosis from a specific specimen. However, the generalisability of the data across groups of patients for audit purposes was questionable. Standardisation of recording was not assured.

Thus, the hospitals' data was of variable quality; coding was not consistent and was not usually compatible with the other data. After attempting to identify practical solutions to these problems a decision was made not to interrogate the data further or attempt to validate and integrate it, but to accept that the study would be essentially limited to the HES and Exeter data already obtained. Chapter 4.6.1 has outlined in greater detail the justification for this decision.

Table 32. Summary of hospital laboratory data obtained

Unit Number of HES cases	Hospital A 412	Hospitals B & C 412	Hospital C 164
Records obtained	923	2,103	215
DOB	✓	✓	✓
Postcode	X	X	X
NHS No	✓ (93.2%)	✓ (99%)	✓ (83%)
Hospital No	✓	✓	✓
Date received at lab	X	X	X
Date reported	✓	X	✓
Sample ID	✓	✓	✓
Clinician	✓	✓	X
Source of specimen	✓	✓	X
Tissue Type - T code	✓	✓	✓
Number of possible T Codes	2	6	6
Procedure at which obtained	X	X	X
Result - M code	✓	✓	✓ - free text only
Number of possible M codes	2	6	6
Free text	✓	X	X
Notes	Telepath with Excel output, file of 3,236 lines generated with data on ALL women who had any gynae procedure during the study year. Had to be cleansed significantly but resulting file of 923 still impossible to match with great accuracy.	Telepath with Excel output. Another large file of 4,450 lines representing 3,834 NHS numbers. Matching erratic.	Excel file generated by lab: 2,377 records, once converted to one woman per line these related to almost the same number of women in HES database, but did not match well also morphology results not coded - just free text.

5.5 CODING OF FINAL MERGED DATABASE

Before full analysis of the database could be undertaken, various key data items needed to be grouped and coded or re-coded to permit meaningful statistical testing. The following section outlines the major areas of re-coding that were undertaken and attempts to justify the categories and groupings that were applied. Particular attention is given to the most significant diagnosis attributed to each study participant at time of hysterectomy; what type of hysterectomy she underwent (total or subtotal); whether or not she had cervical screening prior to surgery ('screening history'); whether or not she had any follow-up vault cytology and if this was appropriate according to national guidelines.

5.5.1 Postcode and the addition of deprivation indices

Postcode is a highly specific identifier of a patient's address and deprivation score. The 6,141 supplied postcodes were in 'Postcode 8' format, meaning that every postcode was made up of eight characters including spaces so the University of Birmingham would be recorded as 'B15--2TT', but the Bullring shopping centre in central Birmingham is recorded as 'B5---4BU', where - represents a space.

Before deprivation indices could be derived from these postcodes the spaces had to be removed; achieved using the 'Find and Replace' function in Excel. Then, using the Midlands Research Practices Consortium (MidREC) postcode database (2.5 million entries, in Access), the fields listed in Table 33 were added via a 'merge query', as a set of new columns with an entry for each postcode provided.

The postcode database is a resource that is regularly updated by staff from MidREC based at the University of Birmingham and is derived from the National Statistics website and National Administrative code service.

Table 33. Deprivation and geographical indices derived from postcode

Code	Name	Notes
SOA1	Super Output Area 1	The 'lower layer Super Output Area code' for each postcode (Eng & Wales)
SOAPopCt	SOA Population Count	Actual number of inhabitants of that SOA in 2007
IMD07Score	IMD2007 Score	Index of Multiple Deprivation 2007 actual score
IMD07Rk	IMD2007 rank	Index of Multiple Deprivation 2007 rank
Town01Score	Townsend 01 score	Townsend 2001 actual score
Town01Quin	Townsend 01 Quintile	Townsend 2001 quintile
Town01Rk	Townsend 01 Rank	Townsend 2001 rank

The decision was taken to use IMD07 rather than Townsend scores throughout this study as IMD is now regarded as being a more sophisticated measure.[155] Index of multiple deprivation 2007 (IMD07) is a comprehensive, robust measure which uses seven main indices to assess deprivation: Income, Employment, Health & Disability, Education, Barriers to Housing & Services, Living Environment and Crime, which together incorporate 38 items.[156]

IMD07 works at the level of Lower Super Output Areas (LSOAs). There are 32,482 of these LSOA's in England, each with an average population of 1,500 people (range 1000 - 3000). The LSOA ranked 1 is the most deprived in England, with the one ranked 32,482 the least deprived.

This latest index is based on information from the 2001 census and on the latest available data, in some cases averaged from 2003-2005.[157] As the most detailed deprivation indicator available it is used to highlight variation between areas and provides a relative (rather than absolute) ranking, thus the score is not linear. Of note, IMD07 is not an index of affluence, but of deprivation, thus a high ranking score does not necessarily mean an affluent area, rather that there is an absence of deprivation, a subtle but important difference. Detailed IMD data is available for the West Midlands region.[158]

5.5.2 Diagnosis coding

The ICD10 codes from HES (DIAG codes) provided the study population with a set of specific diagnoses at the time of surgery and this permitted women to be classified into having benign (non-cancerous), intermediate (pre-malignant or borderline malignant) or malignant (invasive) disease. Section 5.2.2 outlined the numbers of codes; the majority of women had just two but the maximum for any study participant was 11. Table 34 summarises the first level re-coding that was undertaken, whereby all the DIAG codes were grouped into one of 15 categories, these were then grouped and reclassified into a simpler grouping for each individual woman whereby the 'worst' of her various diagnosis codes was taken and used to put her into one of four diagnosis bands; benign, pre-invasive, malignant disease or unknown. Appendix J includes further detail of the re-coding.

Table 34. First level re-coding of HES diagnosis codes

ICD10 Section	Recode options	Notes
A - B: Certain infectious and parasitic diseases	1: Of no interest to study 2: HIV malignancy 17: Gynae, infection	*Sexually transmitted diseases were put with gynaecological diseases but HIV related malignancy was allocated to section 2 to allow for comparisons with other malignancies*
C - D50: Neoplasms	2: Non-gynae malignant 5: Non-gynae, benign 12: Gynae malignant 15: Gynae benign	*This whole chapter allocated to new growths, both malignant and benign: C51-C58 malignant neoplasms of female genital organs: D39= neoplasm of uncertain behaviour of the female*
D50 - 99: Diseases of the blood	1: Of no interest to study	*All grouped as of being unrelated to the study and as such excluded from analysis/comparisons*
E: Endocrine, nutritional and metabolic diseases	1: Of no interest to study	
F: Mental and behavioural	1: Of no interest to study	
G: Nervous system	1: Of no interest to study	
H: Eye & Ear	1: Of no interest to study	
I - J : Circulation & respiratory	1: Of no interest to study	
K: Digestive	1: Of no interest to study	
L - M: Skin & Muscle	1: Of no interest to study	
N: Genitourinary	1: Of no interest to study 16: Gynae, inflammation 18: Gynae, bleeding 19: Gynae, other	*N70-98 all other gynaecological diagnoses*
O: Obstetric	10: Obstetric general 15: Gynae benign 19: Miscarriages (other gynae)	*O01.9 Chorioadenoma (hydatidiform mole) was one specific example of a benign obsetric tumour*
Q: Congenital	1: Of no interest to study	
R : Not otherwise classified	88: Non diagnostic	*Descriptive terms, not diagnosis thus no contribution toward study aims*
S - T: Injury etc	88: Non diagnostic	
W - Y: 'External causes'	88: Non diagnostic	
Z: Factors influencing health contacts	88: Non diagnostic	
Missing data	99: Missing	*For blank cells*

5.5.3 Operation type coding

It was important, if the aims of the study were to be realised, to establish which type of hysterectomy each woman had undergone: a sub-total hysterectomy, when some of the cervix is retained at time of surgery, is an indication for continued participation in the national cervical screening programme. Whereas, a total hysterectomy, where all the cervix is excised, means that a woman is no longer eligible for continued participation in cervical screening; she may however, fit the criteria for follow-up by means of vaginal vault cytology.

The OPERTN codes in HES, which utilise OPCS4 (see section 3.2.2.2), were used to determine which operation was performed on each woman and a code applied accordingly. However, before allocation into hysterectomy type could be undertaken, it was necessary to first establish which operation codes may be of relevance to the study and so all the OPERTN codes were recoded, in SPSS, into one of the following operation groupings: breast, gastrointestinal, genitourinary, vaginal or prolapse, other gynaecological, obstetric or other. Table 35 summarises this re-coding.

All women had their 'hysterectomy' operation code established and classified into one of the following three groups: total hysterectomy (to include abdominal, vaginal or laparoscopically assisted), sub-total hysterectomy and unknown (where OPCS coding was generic and did not specify operation variant).

Table 35. Re-coding of OPCS codes

Meaning of grouped OPCS codes	Number	% of all codes
Breast surgery	**11**	0.08
Abdominal or GI tract surgery	**1,408**	10.80
Genito-urinary or bladder surgery	**401**	3.08
Vaginal or prolapse surgery	**1,130**	8.67
Gynaecological surgery	**10,057**	77.14
Obstetric surgery	**31**	0.24
Total of useful codes (1-6)	***13,038***	***100***

For women who had several operation codes it was sometimes possible to allocate them manually to the total or sub-total hysterectomy groups from the 'unknown' category to 'total', by establishing either that the cervix was excised or that vaginal surgery had taken place. However, a small proportion of cases remained where it was impossible to be certain; these were retained in the study population but were treated as a separate group for some of the analysis (specified in the Results, Chapter 6).

5.5.4 Cytology screening history

5.5.4.1 Total number of cytology tests

The first step in classification of each woman's personal screening history was to establish how many cytology tests she had undergone. It was assumed, for the purposes of the study, that if a woman could not be found on the Exeter system, despite electronic and extensive manual searching, that she did not have any cervical screening history. However, many women who definitely never had any cytology were included in the Exeter system because this suite of software is used for many different healthcare applications, not just the national cervical screening programme.

For women not recorded in Exeter, it was possible that some were relatively new immigrants to the UK when they developed problems necessitating gynaecological surgery. As such they may not have been fully registered on the Exeter system, although new registration with any GP surgery should automatically trigger registration.

Some operations would have been undertaken as emergencies i.e. whilst women away from home, and it is known that a number of illegal immigrants in the UK deliberately try to stay 'below the radar' of Primary Care services and just present directly to secondary care when they have acute healthcare needs.

A simple count of all the tests ever recorded for each woman was made and used as a reference for further classifications.

5.5.4.2 Differentiation between pre and post operative cytology

By using each woman's first operation date as the critical 'event' date it was possible to compare the date of every cytology test with this and allocate it to being pre or post operative. It was then possible to count how many of each type of test every woman had ever had.

5.5.4.3 Last smear before operation - 'Index test':

This was determined using the operative date, as above, and this test was renamed the 'index' test i.e. the test that may have indicated a need for surgery.

5.5.4.4 Full screening history prior to surgery: WMQARC algorithm classification

There were a wide range of cervical screening history patterns evident in the data, too many to allow for meaningful comparisons and so a decision was made to use a pre-existing algorithm, developed by the West Midlands Cancer Intelligence Unit, Quality Assurance Reference Centre (WMQARC). It was anticipated that use of this coding would allow for future collaborative working.

This algorithm was applied to the data as described in Chapter 4. The resulting two new columns of data included a 'screening status' code which outlined at what stage the event (hysterectomy) had occurred in relation to the routine screening programme (eight categories) and a 'screening history' code.

This screening history code was a five integer categorisation with each integer representing a different 'layer'. Details of this algorithm are outlined in Journal of Medical Screening, 2006.[111] In essence the main 'layers' are: whether or not a woman had ever attended for screening, when the index smear was taken in relation to the hysterectomy operation and what the result of that test was, then all the tests in the entire history are considered to see if any have been abnormal (and to what degree) and if a woman has ever been suspended from the programme.

The 6,141 women from the merged HES/Exeter database all had their Exeter data run through the algorithm. This resulted in 228 different screening codes being applied. This was too complex to allow for meaningful analysis and so it was essential to re-code. These 228 codes were strings of integers rather than meaningful numbers thus the strings were split into their 5 component integers; in the case of four integer strings, a zero was used as the first integer (Table 36).

Table 36. Description of 5 integers of screening history classification

Integer	Meaning	Options
1st	Whether or not ever attended for screening and if age is related to this	0 - 5, 9
2nd	Time of the most recent screening smear test compared to hysterectomy operation	1 - 5
3rd	The Index test - description of the last test prior to hysterectomy	1 - 6
4th	All other smear tests - were any bad enough for recall to be suspended?	1 - 6
5th	Either, if 4th not bad, were they ever abnormal OR if 4th bad, what type?	1 - 4

An important step was to identify those groups of women who had had abnormal cytology results just prior to hysterectomy (index test) or ever, and then to be able to compare them with those who had never had abnormal cytology.

Rather than use the classification to establish which women had ever attended for screening, the study database permitted quicker classification thus the first integer of the code was not of great relevance.

The timing of the index smear in relation to the hysterectomy could be examined separately by just using integer two (no need for re-coding). Thus the third integer was used for the first block of re-coding, to split women thus:

- Group 1 - Index smear significantly abnormal
- Group 2 - Index smear uncertain (borderline, inadequate, glandular)
- Group 3 - Index test normal
- Group 4 - Never had any tests done

Then the fourth and fifth integers were used to establish the remainder of the screening history and women could finally be categorised into the 13 groups, summarised in Table 37; a more complete table of this recoding is available as Appendix K.

Table 37. Summary of re-coding of screening history before hysterectomy

Main Group	Full Code	Explanation
1	11	Index abnormal, previous history includes abnormal tests
	13	Index abnormal, previous history only ever normal
	18	Index abnormal, previous history includes tests of uncertain significance
	19	Index abnormal, only one test pre-op
2	31	Index normal, previous history includes abnormal tests
	33	Index normal, previous history all normal
	38	Index normal, previous history includes tests of uncertain significance
	39	Index normal, only one test pre-op
3	81	Index of uncertain significance, previous history includes abnormal tests
	83	Index of uncertain significance, previous history only ever normal
	88	Index of uncertain significance, previous history includes uncertain test results
	89	Index of uncertain significance, only 1 pre-operative test
4	99	Never had any pre-op testing, or at least nil recorded in Exeter or too old to have ever been detected in programme (even if did have smears)

5.5.5 Vaginal vault cytology testing and its appropriateness

Once women had been categorised in to their hysterectomy type, severity of disease at time of hysterectomy and whether or not each of their cytology tests took place prior or subsequent to surgery, it was possible to give each participant a code for the appropriateness, or otherwise, of her having vault cytology testing.

Table 38 summarises the two levels of 'appropriateness' categorisation used; a 'crude' set of categories, having three groups and a 'complex' set, having five groups and also the number of women falling into each category. The table also includes a 'group' code which refers to the main diagnosis and whether or not any post-operative cytology testing took place.

5.5.6 Other data items generated or coded

Age at operation

Age, in years, on the day of surgery was calculated as the difference between operation date and date of birth, divided by 365.25. As well as being available as a discrete number, age was grouped into five-year bands, with the extremes being <20 years and >90 years, giving 16 categories for use in some of the analysis.

Ethnicity

Ethnicity was further coded, from the 16 main groups originally supplied by HES, to a simpler six grouping system (white, mixed, Asian, black, Chinese, other) to facilitate some analysis as the numbers of women in the various sub-groups was very small. Indeed it was further necessary to divide women into White, non-white and not specified, for some analysis.

Table 38. Summary of diagnosis and cytology coding to establish appropriateness of post operative cytology

Subgroup (Operation type and main diagnosis)	Group code	Crude code*	Complex code**
Total Hysterectomies = 5,697			
Malignancy, no post op cytology	**A**	**9**	**30**
Malignancy, post op vault smear tests done	**B**	**9**	**31**
CIN or Carcinoma in situ, no post op cytology	**C**	**0**	**20**
CIN or Carcinoma in situ, post op vault smear tests done exact to protocol	**D**	**1**	**21**
CIN or Carcinoma in situ, post op vault smear tests done but too many (>2 in 2yrs)	**D**	**1**	**22**
CIN or Carcinoma in situ, post op vault smear tests done but too few (1 only in 2yrs)	**D**	**1**	**23**
CIN or Carcinoma in situ, post op vault smear tests done but outside recommended window (>18m)	**D**	**1**	**24**
Benign disease, no post op cytology	**E**	**1**	**11**
Benign disease, no post op cytology, <10yr FUp before op (age less than 35yrs)	**E**	**1**	**12**
Benign disease, post op vault smear tests done thus inappropriate	**F**	**0**	**10**
Benign disease, post op vault smear tests done: <10yr FUp before op (age less than 35yrs), just one smear so appropriate but post 2004 guidelines	**F**	**0**	**15**
Benign disease, post op vault smear tests done: <10yr FUp before op (age less than 35yrs) but >1 smear so still inappropriate	**F**	**0**	**16**
Unknown diagnosis, no post op cytology	**G**	**9**	**80**
Unknown diagnosis, post op vault smear tests done	**H**	**9**	**81**
Subtotal Hysterectomies or unspecified total = 444			
Malignancy, no post op cytology	**J**	**9**	**98**
Malignancy, post op cytology tests done	**K**	**9**	**99**
CIN or Carcinoma in situ, no post op cytology	**L**	**0**	**90**
CIN or Carcinoma in situ, post op cytology tests done	**M**	**1**	**91**
Benign disease, no post op cytology	**N**	**0**	**90**
Benign disease, post op cytology tests done	**P**	**1**	**91**
Unknown diagnosis, no post op cytology	**Q**	**9**	**98**
Unknown diagnosis, post op cytology tests done	**R**	**9**	**99**

* 1= Correct, 0 = Not to protocol, 9 = N/A

** 1# = Benign, 2# = CIN, 3# = Cancer, 8# = Unknown, 9# = Not vault

5.6 SUMMARY OF CHAPTER

This chapter has outlined how the study data was managed: validation of the data from HES included calculating missing dates i.e. of duration of hospital stay post-operatively and decision making concerning handling of errors or missing data i.e. erroneous coding of site of treatment for three of the hospitals in the West Midlands. One significant concern during data validation was the lack of consistency in recording a patient's self-declared ethnicity; this was only present in 68.5% of records from HES. Apart from this notable exception, the data from HES was felt to be comprehensive and valid.

The data received from the 'Exeter' sources was similarly of high quality and comprehensive, however a lot of irrelevant data was obtained which was discarded. Obtaining valid postcodes was challenging, as it was not held as a separate field, rather as a string at the end of the patient's address. However, once extracted from this string of data it was present consistently and accurately.

The data obtained from some of the hospitals was very disappointing. There was no standardisation across the various sites with respect to software used or even coding of data. Some sites used out-dated nomenclature and although 'translation' was considered, a decision was made that comparisons between hospitals should not be attempted as the data was too unreliable.

Overall the quality of data from HES and Exeter exceeded the expectations of the study protocol, however the hospital level data was poor for the purposes of this study and the decision was made not to attempt to incorporate this into the main database as it may invalidate the study findings.

Coding of several data items was undertaken prior to commencement of any analysis. In particular, transforming the national coding for operations (OPCS) and diagnosis (ICD10) into groups relevant to the aims of the study had to be performed. Entire cytology screening history was considered and summarised with tests being classified into having occurred pre or post hysterectomy.

An algorithm designed for use in the WMQARC was applied to women's entire screening histories, this generated a complex series of codes and so these were further categorised according to the study aims to permit appropriate comparisons.

Finally, data concerning vaginal vault cytology was scrutinised and an assessment of 'appropriateness' according to national guidelines was made. Thus, every woman had a set of data which was available for interrogation which summarised her hysterectomy operation (i.e. when, where, what type of operation, what was the final diagnosis?), her entire cervical screening history before surgery (i.e. how many tests and when were they done, what were the results of each?) and any screening in the four years subsequent to surgery (i.e. how many tests performed, what were the test results, was screening undertaken in accordance with national guidelines?).

CHAPTER SIX: RESULTS

INTRODUCTION TO CHAPTER

This chapter presents the results of the analysis of the study database, which are relevant to the study aims, and summarises the main study findings in four main sections. Starting with an overview of the demographics of the whole study population: 'who' the study participants were including their age, deprivation, ethnicity and cervical screening history prior to surgery. Then exploring 'Why' these women underwent a hysterectomy operation; examining their entire cervical screening history prior to surgery and focussing on the last test preoperatively (the index test).

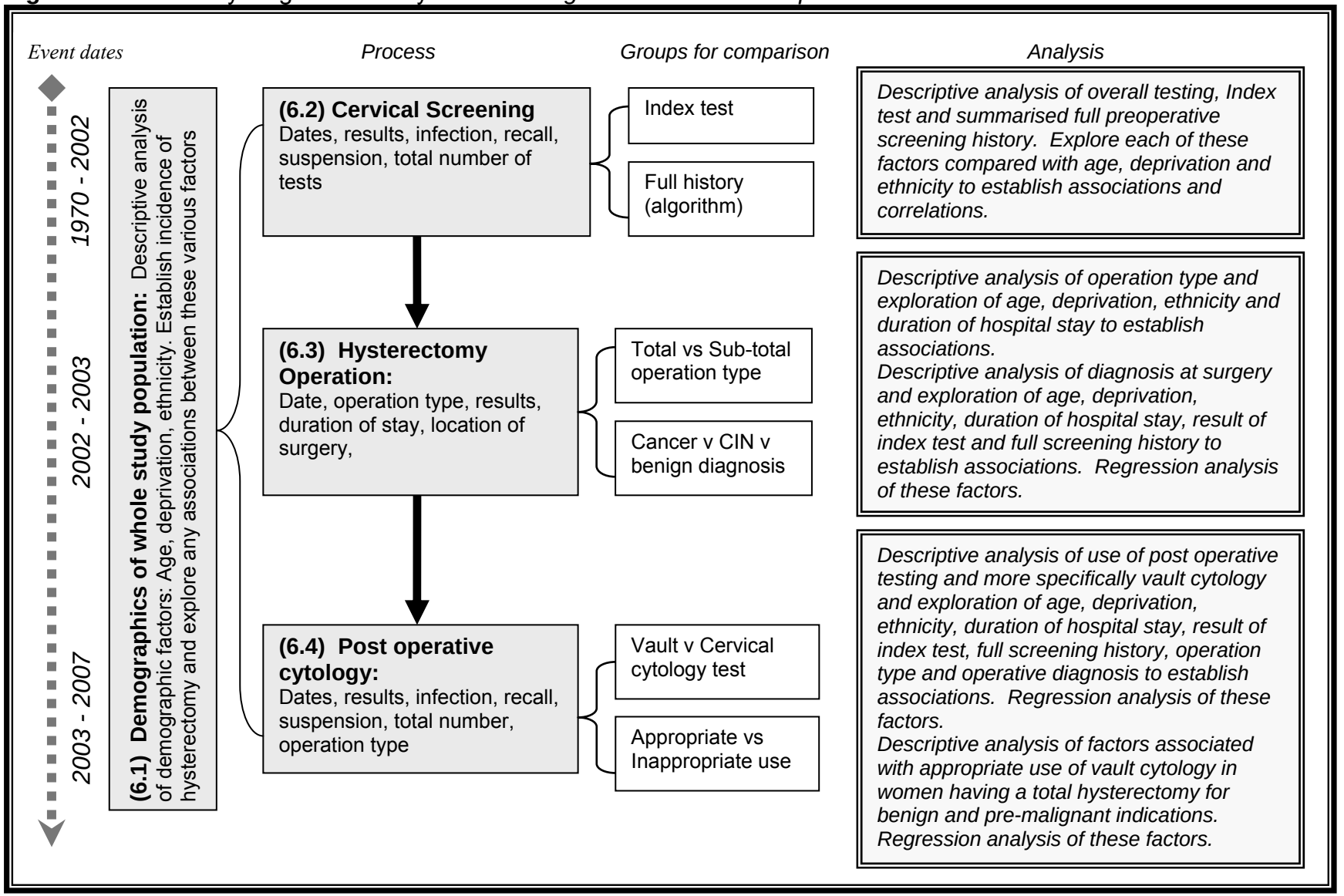
The chapter then goes on to establish what the operative diagnosis was, for each woman, what type of hysterectomy operation she had and exploring the factors influencing this. The analysis concludes, by exploring 'What happened next' by looking at those women who had vaginal vault cytology tests subsequent to surgery. This sub-group is contrasted with the rest of the study population to establish whether or not this testing was appropriate or justified, according to national guidelines. Figure 17 illustrates and summarises these four main stages of analysis including the main groups that are examined and the comparisons undertaken at each stage. Figure 17 also demonstrated how all the data are all related chronologically through the 'patient journey'. Section numbers included in this figure relate to the main chapter sections to facilitate navigation.

Finally, the chapter summary brings together some of the key findings of the four main stages of the analysis.

Throughout the chapter, the value of 'p' is always stated, rather than assuming any particular value to be 'statistically significant'.[159] The clinical significance or relevance of all findings and the potential for bias are then discussed in the subsequent chapter. Percentages are usually quoted to two decimal places, whereas other calculations and statistical test results are quoted to three decimal places. Degrees of freedom are expressed as #df throughout. Confidence intervals (CI) around proportions represent the 95% range and were calculated using the exact method throughout; they always quoted to at least two decimal places, if they are given in a table, they are usually omitted from the text, for clarity.

Wherever box plots are used throughout the chapter, the horizontal line represents the median, the boxes represent the interquartile range (IQR), the bars represent the upper quartile plus (IQR x 1.5) and the lower quartile minus (IQR x 1.5).[149] For histograms the vertical axis (y) is the count or total unless otherwise specified.

Figure 17. Summary diagram of analysis. *Including section numbers in parenthesis*



6.1 CHARACTERISTICS OF THE STUDY POPULATION: DEMOGRAPHIC INFORMATION ABOUT WOMEN HAVING A HYSTERECTOMY OPERATION

6.1.1 Summary of demographic data

Table 39 summarises the key demographic characteristics of the study population of 6,141 women who were resident in the West Midlands area and who had a hysterectomy performed between 1st April 2002 and 31st March 2003. The rest of section 6.1 examines these further.

Table 39. Summary of demographic characteristics of study population

Population Variable	Results	Notes
Incidence of hysterectomy	23 per 10,000 women, per annum (crude and adjusted rates)	Equates to approximately 7 cases per annum for a typical GP surgery. Age adjustment did not substantially alter the overall rate 22.81 vs 22.96 per 10,000pa. Thus crude rates used throughout. Significant variation in incidence, according to age, peak of 63 per 10,000pa in the 45-49 years old group.
Age of population at date of operation N = 6,141	Range: 17 - 94yrs Mean 51.12, SD 13.11 Median 48.38, IQR = 18.21	Not normally distributed, skew to right, Skewness = 0.606. Kolmogorov-Smirnov = 0.088, df 6,141, p<0.001.
Deprivation (IMD07) Quintiles: 1. (Deprived) =1,628 2. = 1,210 3. = 1,295 4. = 1,177 5. = 831	Study population very similar to West Mids in terms of deprivation. However, significantly different from England as a whole.	IMD07 quintiles of study population were compared with the population of England ($\chi 2$ = 263.577, 4 df, p<0.001) Worsening deprivation was associated with increased incidence of hysterectomy, age adjusted trend = -0.99, p = 0.001, most deprived 25.17 per 10,000pa, least deprived 19.97 per 10,000pa.
Ethnicity N = 4,213 White = 3,842 Mixed = 15 Asian = 209 Black = 119 Other = 28	White British = 86.4%, very similar to West Midlands (86.5%). Asian under represented Black over represented (p<0.001).	Ethnicity data only available for 69% of population. Even allowing for inter hospital variability in coding significant differences between the various ethnic groups existed. Incidence of hysterectomy varied by ethnicity (White 19.67, Asian 15.68, Black 28.01 using provided data only) Age adjustment made little difference. Crude data presented hereafter.

Table 39 cont:

Number of cervical cytology tests ever N = 6,141	36,151 tests Range 0 - 31 tests Mean = 5.89 Median = 6, IQR = 4 - 7 Skewness = 1.050 338 women never had any 23 women ≥ 20	A woman who completes full screening according to current guidelines (25-65yrs) could have up to twelve tests performed but few women do because of pregnancies and also the screening programme only became nationally implemented in the late 1980s. 90% undertaken in primary care. Distribution skewed to the right.
Number of cytology tests preoperatively N = 5,787	34,174 tests in 5,787 women Range 1 - 25 tests Mean = 5.91 Median = 5 IQR = 4 - 7	94.5% of all cytology tests recorded on this population were undertaken pre-operatively.
Number of cytology tests post hysterectomy N = 1,016	1,977 tests in 1,016 women, Range 1 - 10 tests Mean = 1.95 Median = 1 IQR = 1 - 2 16 only had post op testing	National guidelines concerning use of post operative cytology do not apply to women who had malignant disease, just benign or completely excised pre-invasive.
Duration of hospital stay post operatively N = 6,136	Range = 0 - 81 days Mean = 5.06 days SD = 3.115 SEM = 0.04 Median = 5 Mode = 4, IQR = 4 - 5 Skewness = 6.781	Mean duration of entire in-patient stay = 5.9 days, thus less than one day in hospital preoperatively, on average.
Destination on discharge from hospital N = 6,099 Home = 6,027 Died = 10	98% discharged to usual place of residence. 10 died (0.16%)	A supplementary database from HES suggested that 70 women from the study cohort had died during their first year after surgery. However this could not be independently verified as there were no linking identifiers supplied and no cause of death supplied.

Thus it may be seen that our cohort had a hysterectomy incidence of 23 per 10,000 women per annum. They are representative of the West Midlands region in terms of overall ethnicity and deprivation. The average age of the population is consistent with that of women typically undergoing a hysterectomy operation[1] in the UK, and overall these women participated in national cervical screening at a level that seems consistent with national guidelines.

6.1.2 Incidence of hysterectomy operation in the West Midlands

There were 6,141 women resident in the West Midlands region that underwent some form of hysterectomy operation in the study period (1st April 2002 – 31st March 2003) as summarised in Table 39. The total population of the West Midlands region in 2001, from the last census data, was 5,267,308. Women comprised 2,692,197 (51.1%).[124]

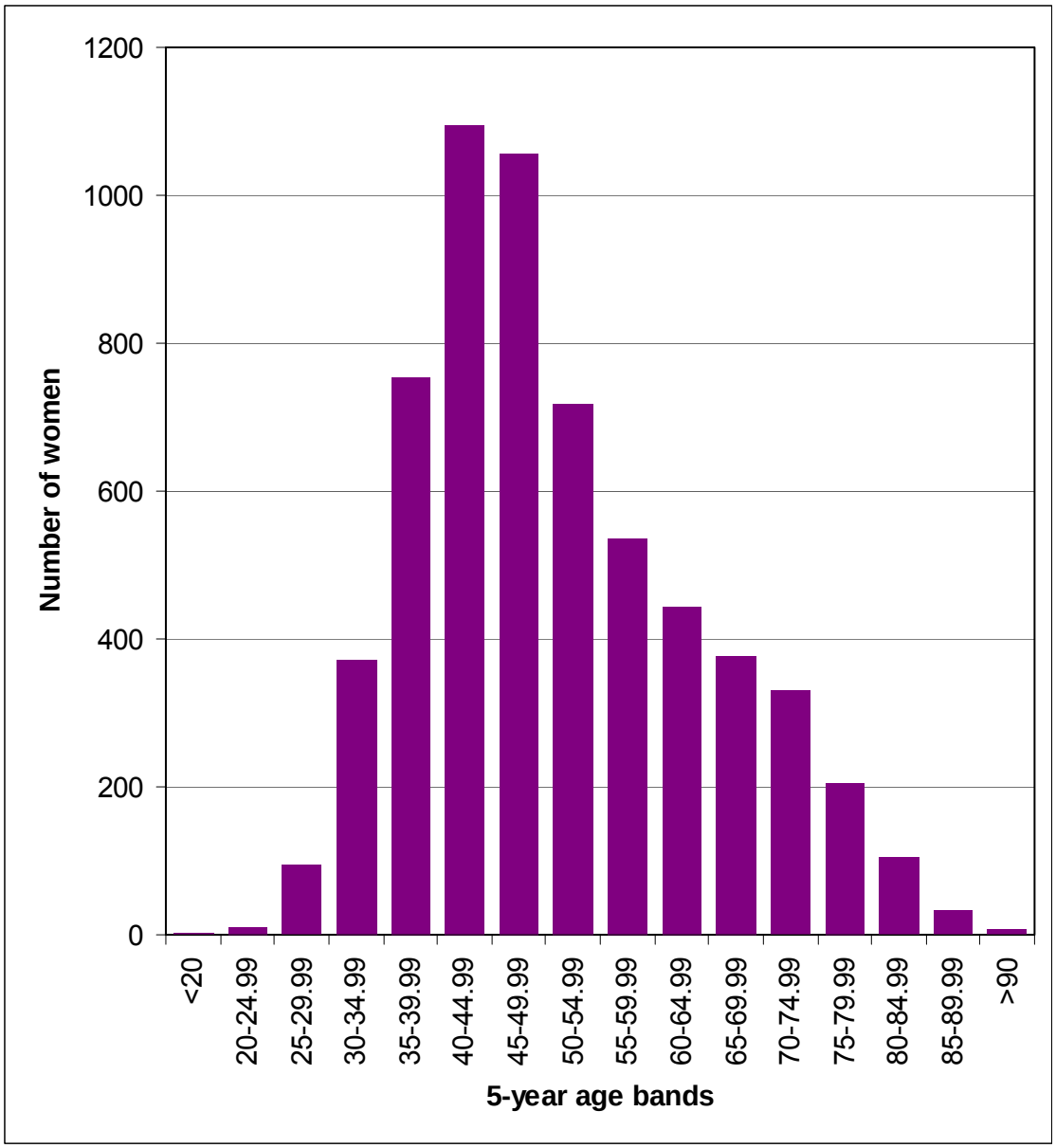
Thus, the crude annual incidence of hysterectomy was 0.23% (*0.222 - 0.234*), or 23 hysterectomies per 10,000 women per annum (0.12% or 12 hysterectomies per 10,000 head of population, male and female).

It is reasonable to anticipate that a typical GP surgery, of around 6,000 patients,[160] could anticipate seven women having a hysterectomy operation in any given year. Thus, the cumulative number of women potentially being eligible for post-operative follow-up in such a typical size surgery, could be in excess of a hundred women, and up to two hundred (seven women per annum, for several decades).[124]

6.1.3 Age of population

The mean age of the 6,141 women, on the day of their hysterectomy operation, was 51.12 years, with a range of 17 - 94 years (SD 13.118yrs). The median age was 48.38 years, with the distribution skewed to the right, see Figure 18, which has the women grouped into five-year bands, for clarity.

Figure 18 Age at operation



The Kolmogorov-Smirnov test for normality was applied to the age data and confirmed that population age is not normally distributed (Test statistic = 0.088, df 6,141, $p<0.001$).

The age specific incidence rates for hysterectomy were calculated using the West Midlands population figures from the 2001 census as a baseline.[124] Table 40 includes these data, it may be seen that the age specific incidence varied from 0.1 per 10,000 women in the youngest group (which only included two women) to 63 per 10,000 in the 45-49 year old group, where the peak incidence has been illustrated in Figure 18.

Table 40. Age specific incidence of hysterectomy (crude incidences)

Group	Age range	Study	W Mids Population (Women)	England population (Women)	WMids as a percentage of England population	WMids Crude Incidence per 10,000 women*
1	16-19	2	131,644	1,177,991	11.18	**0.15**
2	20-24	9	155,028	1,483,873	10.45	**0.58**
3	25-29	94	165,778	1,665,176	9.96	**5.67**
4	30-34	373	198,808	1,928,557	10.31	**18.76**
5	35-39	755	202,026	1,965,187	10.28	**37.37**
6	40-44	1,094	180,620	1,741,553	10.37	**60.57**
7	45-49	1,057	166,914	1,569,632	10.63	**63.33**
8	50-54	719	180,109	1,705,408	10.56	**39.92**
9	55-59	535	156,627	1,405,973	11.14	**34.16**
10	60-64	443	134,727	1,217,373	11.07	**32.88**
11	65-69	378	122,347	1,119,370	10.93	**30.90**
12	70-74	330	115,793	1,062,021	10.90	**28.50**
13	75-79	205	103,283	957,878	10.78	**19.85**
14	80-84	106	74,903	696,973	10.75	**14.15**
15	85-89	33	45,171	444,118	10.17	**7.31**
16	>90	8	23,585	244,884	9.63	**3.39**
Totals		**6,141**	**2,692,197**	**25,216,687**	**10.68**	**22.81**

The study population of women all lived in the West Midlands region, however to ensure generalisability of the study data to the UK, the cohort was age standardised (Direct method)[161] to the population of England using the most recent census data (2001) which is also included in Table 2. The age standardised incidence rate for hysterectomy was 22.96 per 10,000, compared with a crude rate of 22.81, thus the difference was small and crude rates are used hereafter.

6.1.4 Deprivation of the study population and incidence of hysterectomy

Postcode for all the study participants was available from HES and was used to apply a deprivation score for each woman prior to anonymisation. The Index of Multiple Derivation 2007 (IMD07), published by the Department for Communities and Local Government late in 2007, covers the whole of England and was selected for use in this project as being the most robust index available.[157] The reader is reminded that IMD07 is not a measure of affluence, only deprivation and although it is plausible that women living in areas having a very low deprivation score will be more affluent, this does not necessarily follow (see Section 5.5.1).

The IMD07 scores were re-coded into the reference quintiles for England and compared using χ^2 test, giving a score of 263.577, (4 df) and a highly significant $p<0.001$ Thus the study population was considerably more deprived than the UK population generally, summarised in Table 41, where quintile one indicates the most deprived.

This finding is also true of the West Midlands region, which contains 3,482 lower super output areas (LSOAs), of which 27.3% are in the most deprived quintile in the UK, i.e. there is more deprivation in the West Midlands region than in the UK as a whole.[158] Thus, the study population was compared with the West Midlands reference population: χ^2 score 4.192 (4df), p>0.1 which did not suggest a significant difference between the populations, thus the study population was similar to the West Midlands resident population in terms of deprivation.

Table 41. IMD Quintiles for study population

England Quintile	England (reference)	Study Population	% Study *(95% CI)*	% West Mids	Crude Incidence Per 10,000
1 *most deprived*	1,228.2	1,628	26.51 *(25.41-27.61)*	27.28	**30**
2	1,228.2	1,210	19.70 *(18.71-20.69)*	19.59	**23**
3	1,228.2	1,295	21.09 *(20.07-22.11)*	20.36	**24**
4	1,228.2	1,177	19.17 *(18.19-20.15)*	18.81	**22**
5 *least deprived*	1,228.2	831	13.53 *(12.67-14.39)*	13.96	**16**
Total / Aggregated	-	*6,141*	*100*	*100*	***23***

The overall incidence of surgery has been established to be 23 per 10,000 women; for the various quintiles this was then calculated separately and included in Table 41. It may be seen that women in the most deprived quintile were almost twice as likely to have a hysterectomy as those in the least affluent when compared with England as a whole i.e. 30 per 10,000 compared with 16, per 10,000.

To ensure that the observations were valid, age adjustment (Direct method) of the deprivation data was undertaken, Table 42 summarises these data. Although the differences were less pronounced, the previously observed trend was still clearly evident, that women from more deprived areas were significantly more likely to have hysterectomy operations than those from less deprived areas (25 per 10,000 vs 20 per 10,000, test for trend, Pearson = -0.991, p=0.001).

Table 42. IMD Quintiles for study population (age standardised**)**

Age range	*Study*	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
16-19	*2*	1	0	0	0	1
20-24	*9*	5	3	0	0	1
25-29	*94*	40	21	19	8	6
30-34	*373*	128	84	76	53	32
35-39	*755*	246	163	153	116	77
40-44	*1,094*	320	220	216	197	141
45-49	*1,057*	304	199	216	204	134
50-54	*719*	162	137	148	158	114
55-59	*535*	93	92	120	124	106
60-64	*443*	99	68	123	85	68
65-74	*708*	142	153	153	152	108
75-79	*205*	48	41	39	56	21
80-84	*106*	28	22	24	16	16
85-89	*33*	10	5	8	6	4
>90	*8*	2	2	0	2	2
Overall	***6,141***	**1,628**	**1,210**	**1,295**	**1,177**	**831**
Age adjusted per 10,000	***22.96***	**25.17**	**24.04**	**22.93**	**21.95**	**19.97**

6.1.5 Ethnicity of study population

6.1.5.1 Overview of ethnicity

Data on ethnicity of the study population was available from the hospital records (HES) for 4,213 women, representing 68.6% of the population. Of the third of the women with missing data 1,154 had truly missing data but 774 had invalid codes applied (12.6%). Table 43 summarises the collated ethnicity data and also gives the ethnic breakdown of the West Midlands resident population (male and female) in 2001, England and the UK along with the study population. The population data were derived from the last national census in 2001.[124]

6.1.5.2 Ethnicity compared with baseline and UK data

Self declared 'Ethnicity' in the study population was compared with West Midland figures using Chi squared (χ^2) tests. This confirmed that the observed differences exceeded conventional levels of statistical significance ($p<0.05$) for most of the ethnic classifications. In particular, those describing themselves as being of 'other White' background and Caribbean were over represented in the study population, whereas all Asian groups were under represented. The proportion of White British women was almost identical to that locally and they comprised the largest ethnic group (86.4% of study, 86.5% in West Midlands).

It may be seen that the proportion of women of each ethnic group, undergoing hysterectomy, when compared with the ethnic make-up of the general population, is different, Table 43. The χ^2 value for all the groupings was 404.4 (14df, $P<0.001$), thus differences do exist.

Table 43. Self declared ethnicity for study population at time of surgery

Ethnic group **Study N**	% **Coded** N=4,213 *CI*	% **Total** N=6,141 *CI*	**West Mids (2001)** %	**England (2001)** %	**UK (2001)** %	**χ2 W Mids**	**χ2 W Mids** Grouped
British (White) **3,641**	**86.42** *85.39–87.45*	59.29 *58.06 -60.52*	86.5	86.99	92.11	0.004	2.035
Irish (White) **28**	**0.66** *0.42 – 0.90*	0.46 *0.29 -0.63*	1.39	1.27		16.142#	
Any other White background **173**	**4.11** *3.51 – 4.71*	2.82 2.41 -3.23	1.2	2.66		294.251#	
White & Black Caribbean (mix) **12**	**0.28** *0.12 – 0.44*	0.20 0.09 – 0.31	0.76	0.47	1.25	13.930*#	32.637*#
White and Black African (mixed) **1**	**0.02** *-0.02 - 0.06*	0.02 *0 - 0.06*	0.07	0.16			
White & Asian (mixed) **1**	**0.02** *-0.02 - 0.06*	0.02 *0 - 0.06*	0.34	0.37		12.455#	
Any other Mixed background **1**	**0.02** *-0.02 - 0.06*	0.02 *0 - 0.06*	0.22	0.31		7.416#	
Indian (Asian or Asian British) **120**	**2.84** *2.35 – 3.35*	1.95 *1.60 – 2.30*	3.39	2.09	1.94	3.828	32.748*#
Pakistani (Asian or Asian British) **72**	**1.71** *1.32 – 2.10*	1.17 *0.90 – 1.44*	2.93	1.44	1.37	21.785#	
Bangladeshi **7**	**0.17** *0.05 – 0.29*	0.11 *0.03 – 0.19*	0.60	0.56	0.52	13.316#	
Any other Asian background **10**	**0.24** *0.09 – 0.39*	0.16 *0.06 – 0.26*	0.40	0.48	0.45	2.833	
Caribbean (Black or Black British) **91**	**2.16** *1.72 – 2.60*	1.48 *1.18 – 1.78*	1.56	1.14	1.04	9.467#	14.812#
African (Black or Black British) **15**	**0.36** *0.18 – 0.54*	0.24 *0.12 – 0.36*	0.23	0.97	0.90	2.853	
Any other Black background **13**	**0.31** *0.14 – 0.48*	0.21 *0.10 – 0.32*	0.19	0.19	0.18	3.062	
Chinese (other ethnic group) **11**	**0.26** *0.11 – 0.41*	0.18 *0.07 – 0.29*	0.31	0.45	0.46	0.341	0.341
Other **17**	**0.40** *0.21 – 0.59*	0.28 *0.15 – 0.14*	0.27	0.44	0.43	2.722	2.722
Sub-Total, non white ***371***	**8.81** *7.95 – 9.67*	**6.04** *5.44 –6.64*	*10.91*	*9.08*	*7.29*		
Totals ***4,213***	**-**	**-**	**-**	**-**		***404.403 (14 df) p<0.001***	***85.2954 (5df) p<0.001***

* Cells containing less than 5 were merged appropriately to facilitate analysis
# χ^2 <0.05 with 1df for that individual comparison i.e. exceeding conventional statistical significance

To attempt to counteract potential variability between different hospitals coders in the recording of patient's ethnicity data, the six main ethnic groups were merged and then re-compared. It was found that although the differences between the study population and the West Midlands residents were smaller than differences with the UK population, they were all still present and remained highly significant (see final column of Table 43). Thus the χ^2 value for the collated groups was 85.295 (5df, $p<0.001$). These six main groups were used for the remainder of the analysis.

White British women comprised the overwhelming majority of the study population; Figure 19 excludes them to facilitate interpretation of the prevalence of the other ethnic groups. The West Midlands region represents the baseline population from which these women are drawn; however, data for the whole England is also included for comparison.

6.1.5.3 Incidence of hysterectomy for the main ethnic groups (crude and adjusted)

The crude likelihood of women from the main ethnic groups having a hysterectomy operation was calculated, Table 44 demonstrates the wide variation that was noted, with the Black women being more likely than any other group of women to have had a hysterectomy. In those ethnic groups with very small numbers it is difficult to make meaningful comment. This particular table was devised on the assumption that women whose ethnicity was stated (4,213) were in the same proportions as the ethnic distribution of the whole study population (6,141).

Table 44. Incidence of hysterectomy by ethnic group*

Ethnic group	Study N	Study % N = 4,213	UK data	UK data (2001) %	Incidence per 10,000 UK
White (all groups)	3,842	91.19 *90.33 – 92.05*	54,153,898	92.12	23
Mixed races	15	0.36 *0.18 – 0.54*	677,117	1.52	5
Asian (all)	209	4.96 *4.30 – 5.62*	2,331,423	3.97	29
Black (all)	119	2.82 *2.32 – 3.32*	1,148,738	1.95	33
Chinese (other ethnic)	11	0.26 *0.11 – 0.41*	247,403	0.42	14
Other	17	0.40 *0.21 – 0.59*	230,615	0.39	24
Sub-total of non white	*371*	*8.8* *7.95 – 9.67*	*4,635,296*	*7.88*	*25*
Totals / Aggregate	***4,213***	***100***	***58,789,194***	***100***	***23***

** NB These data assume that the ethnicity of the whole study population is in the same proportions as those where it was stated.*

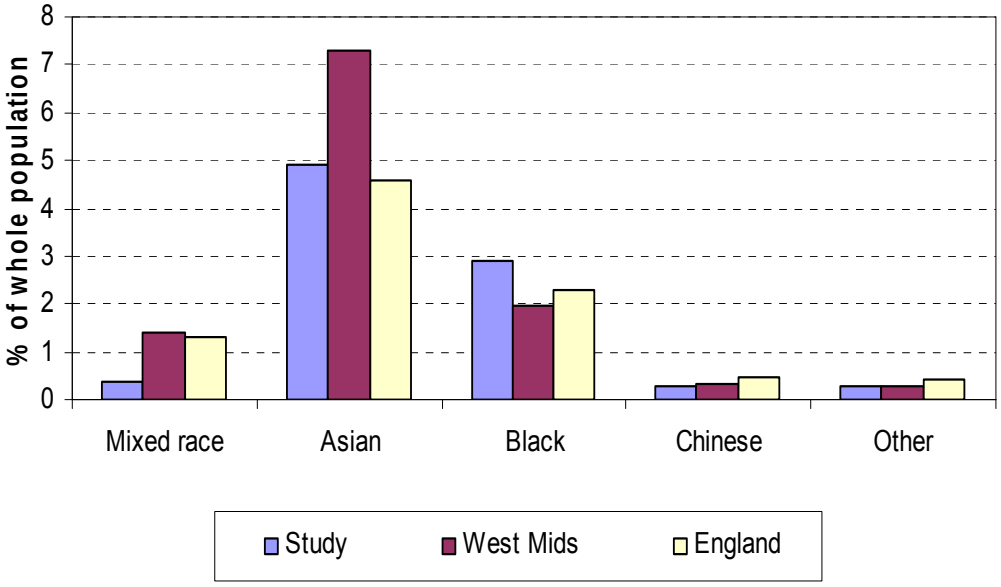
Age standardisation (direct method) of the incidence of hysterectomy in the three largest ethnic groups was undertaken Table 45 & Figure 19). This was calculated only on the given data, rather than assuming the proportions. Invariably rates of hysterectomy were lower (as a third of the study population are excluded), however, valid between group comparisons may still be made. The difference between crude and age standardised incidence rates were very small for White and Black ethnic groups (White: 19.67 vs. 19.50 Black: 28.01 vs. 28.03); for the Asian population this was slightly greater (15.68 vs. 16.39). In view of these findings no further adjustment for age was used.

Table 45: Age standardised incidence for some ethnic groups

Group	Age range	Study Population total	Study Ethnicity stated	West Mids	White	Asian	Black*
1	16-19	2	2	131,644	2	0	0
2	20-24	9	6	155,028	6	0	0
3	25-29	94	74	165,778	70	0	2
4	30-34	373	275	198,808	255	12	7
5	35-39	755	535	202,026	479	22	28
6	40-44	1,094	719	180,620	635	44	31
7	45-49	1,057	690	166,914	597	57	22
8	50-54	719	498	180,109	445	35	13
9	55-59	535	365	156,627	347	13	4
10	60-64	443	311	134,727	293	14	2
11	65-69	378	258	122,347	244	6	6
12	70-74	330	228	115,793	223	3	2
13	75-79	205	146	103,283	142	2	2
14	80-84	106	77	74,903	75	1	0
15	85-89	33	24	45,171	24	0	0
16	>90	8	5	23,585	5	0	0
Totals		**6,141**	**4,213**	**2,692,197**	**3,842**	**209**	**119**
Crude Incidence Rate per 10,000					***19.67***	***15.68***	***28.01***
Direct Standardised Incidence Rate per 10,000*					***19.50***	***16.39***	***28.03***

**The categories of 'other' and 'mixed' ethnicity have been deliberately omitted from the table as numbers were too small to allow for meaningful comparisons.*
*** As a third of the study population did not have ethnicity stated these figures will be significantly lower than the' true' values but do allow for comparison between crude and standardised rates.*
****Direct standardisation against the population of England, 2001 census.*

Figure 19. Study participants and background population compared by ethnic classification



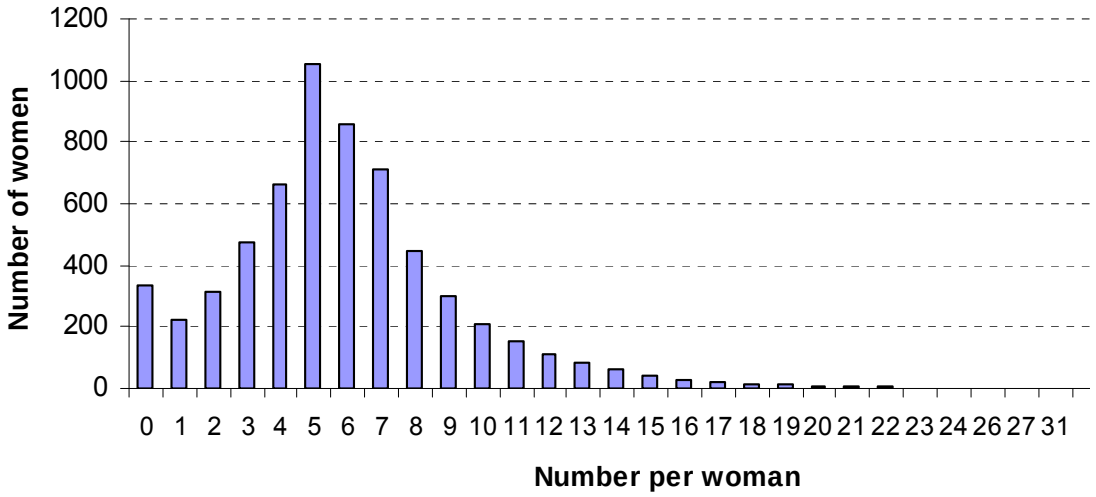
** Excluding White British for clarity*

6.1.6 Overall number of cervical cytology tests

6.1.6.1. Total numbers of cytology tests

6,141 women had 36,151 cytology tests taken and recorded under the national cervical screening programme. With a range of 0 to 31 tests per woman there was considerable variation which, to a certain extent, had been anticipated as older women should have had time to have more tests than younger under the national programme. With a median and mean number of tests of six per woman, and a mode of five, the distribution was skewed to the right (Figure 20, positive skew).

Figure 20 . Total number of screening tests



Of note 90% (*CI 89.25 – 90.75%*) of women had less than 11 cytology tests and 99.6% had less than 20; 23 women having between 20 and 31 tests done. Table 46 includes data on total numbers of tests broken down into 5-year bands and illustrates that there is significant variability in the mean number, with the younger women having less time to have ever had any tests, and the eldest women being too old for the national screening programme and women aged from 40-50 having had the maximal opportunity for routine screening.

Table 46. Total number of tests for each age band of women

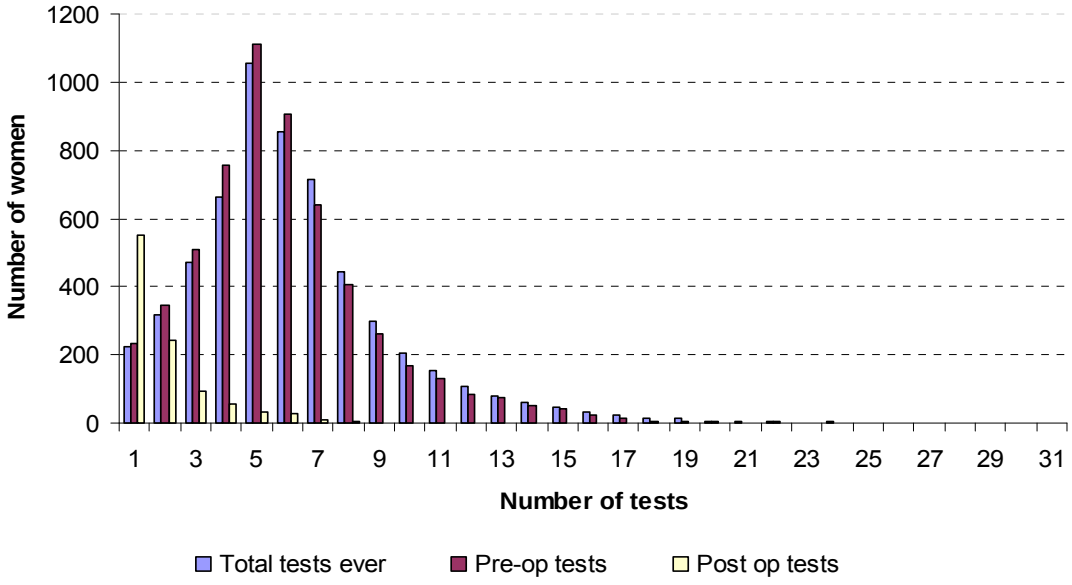
Band	Age Range (yrs)	Number of women	Mean number of tests	Median n. of tests	Range	Standard error
1	<20	2	0	0	0	-
2	21-25	9	4.56	4	0 - 9	1.100
3	26-30	94	4.48	4	0 - 19	0.336
4	31-35	373	5.79	5	0 - 20	0.180
5	36-40	755	6.58	6	0 - 27	0.126
6	41-45	1,094	6.67	6	0 - 24	0.103
7	46-50	1,057	6.52	6	0 - 23	0.098
8	51-55	719	6.40	6	0 - 21	0.122
9	56-60	535	6.74	6	0 - 31	0.163
10	61-65	443	6.17	6	0 - 18	0.145
11	66-70	378	4.95	5	0 - 27	0.156
12	71-75	330	3.36	3	0 - 17	0.149
13	76-80	205	1.93	2	0 - 15	0.139
14	81-85	106	1.03	0	0 - 9	0.158
15	86-90	33	0.48	0	0 - 4	0.169
16	>90	8	0.25	0	0 - 2	0.250

6.1.6.2 Numbers of test pre and post hysterectomy

The tests were then divided into those taken before the main operation date and those taken afterwards: 34,236 were before (94.70%, range 0 - 23 tests) and 1,977 afterwards (5.47%, range 0 - 10), illustrated in Figure 21.

Those women having cytology tests done after hysterectomy, and who had a total hysterectomy (i.e. removal of the cervix uteri) had vaginal vault smear tests or, more correctly, vaginal vault cytology tests taken. These have specific guidelines for their use. Alternatively, women who had retained all or part of their cervix should have remained within the NHS national screening programme and should have had follow-up cytology according to those guidelines, (section 6.4 separates the study population based upon the type of hysterectomy).

Figure 21. Graph of all cytology tests (pre and post surgery)

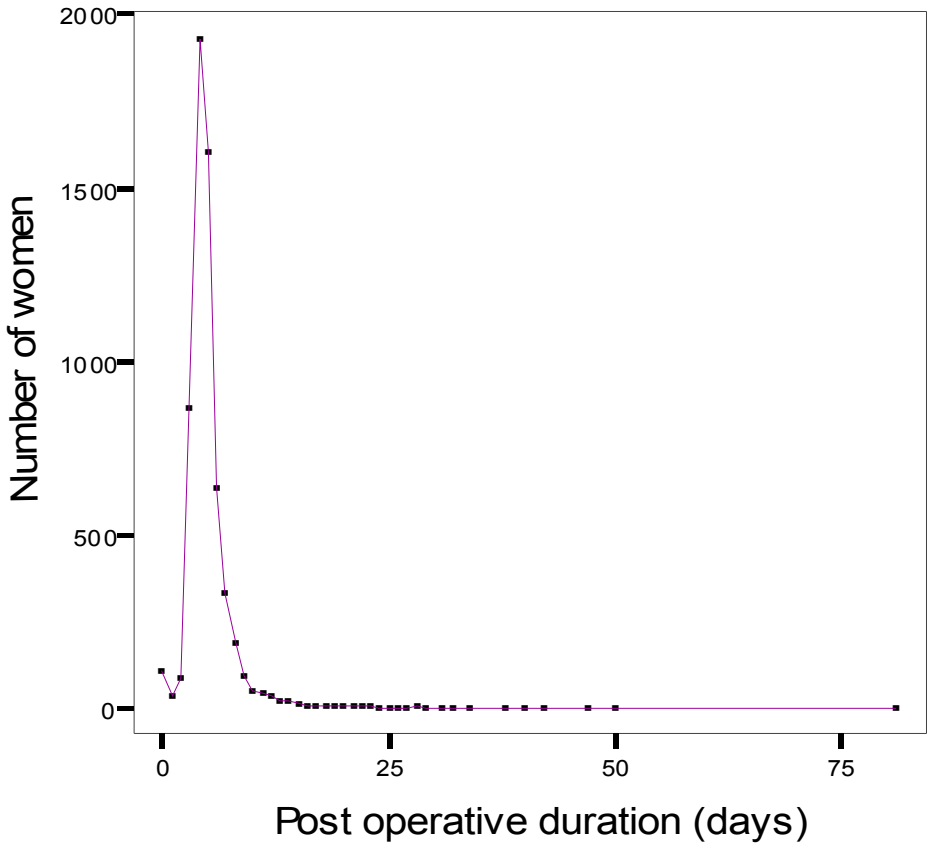


6.1.7 Duration of hospital stay post operatively

The duration of post operative hospital stay was available for 6,136 women and ranged from 0 - 81 days, with a mean duration of 5.06 days (median 5, mode 4 days, inter quartile range (IQR) 4-5 days), Figure 22. 107 women apparently were discharged the same day as their surgery (1.74%, 1.41 – 2.07) and a further 121 (1.97%, 1.62 – 2.32) remained in hospital for one or two days. Only 36 women remained in hospital post operatively for longer than three weeks (0.59%, 0.40 – 0.78).

Total duration of inpatient stay (average = 5.90 days) was calculated as the difference between admission and discharge dates, this differed from post operative stay by the time spent in hospital prior to surgery; this preoperative time averaged 0.87 days and ranged from 0- 72 days with two obviously miscoded dates (giving negative numbers) omitted from the analysis.

Figure 22. Graph of duration of inpatient stay following surgery



Of the women discharged within two days of surgery there was insufficient recording of ethnicity to undertaken meaningful analysis: Of the 228, only 108 had ethnicity codes, of these, 13.9% were of Asian descent and 9.3% were black suggesting these groups may be over-represented.

When grouped into early discharge, (less than three days), normal (3-8days) and late (>8days), there were some differences noted between the groups: living in a less deprived area was associated with early hospital discharge (Pearson χ^2= 17.715, 8df, p=0.023) also being younger was associated with earlier discharge (Pearson χ^2= 345.992, 30df, p=<0.001). These are explored further in subsequent sections (6.1.9.3-4).

6.1.8 Destination on discharge from hospital and in patient deaths

HES data includes where patients state they are going to, on discharge from hospital. Within the study population, in the great majority of cases, this was to their usual place of residence (98.14%). Temporary accommodation was used by 25 women, one went to prison, another to a high security psychiatric unit and ten died (Table 47). When the original data was supplied by HES they also supplied an un-linked file which included details of 70 women (1.14%) from the cohort who had died in the year following their surgery. However, no identifiers were supplied and as such the data could not be further used or analysed.

Patient deaths

Those ten women who died were considered further: six had their ethnicity recorded, five were white British and one was coded as being 'white and Black Caribbean mixed'. Their median age was 69.66 years with the youngest being just 37 years, the eldest was 83 years.

Table 47. Destination on discharge from hospital for study population

Meanings of codes (all possible)	**N**	**%,** *CI*	**Crude rate per 10,000**
Usual place of residence (incl. no fixed abode)	6,027	98.14, *97.86 – 98.42*	9,814.36
Temporary place of residence (i.e. hotels, schools)	25	0.41, *0.28 – 0.54*	40.71
Penal establishment: police station	1	0.02, *0 – 0.05*	1.63
NHS other hospital provider: high security psychiatric	1	0.02, *0 – 0.05*	1.63
NHS ward: general or younger physically disabled.	18	0.29, *0.18 – 0.40*	29.31
NHS ward: maternity patients or neonates	1	0.02, *0 – 0.05*	1.63
NHS run nursing home, residential care or group home	3	0.05, *0 – 0.10*	4.89
Local Authority residential accommodation	11	0.18, *0.09 – 0.27*	17.91
Patient died	10	0.16, *0.08 – 0.24*	16.28
Non NHS institutions i.e. private provider	2	0.03, *0 – 0.07*	3.26
Not applicable	42	0.68, *0.51 – 0.85*	68.39
Total	***6,141***		***10,000***

The hospital stay of women who died was generally protracted, with a median of eight and a half days but a range of two to fifty days. They spanned the whole range of deprivation with women in all five quintiles. Five had cancer as their main diagnoses, four had undergone a hysterectomy for benign indications and one did not have diagnosis information recorded. Four of the five cancers were disseminated disease with secondary spread recorded, two ovarian, one endometrium, one bladder and one where the primary was unknown.

There was not extensive data available concerning underlying medical conditions, but of the five cases without malignant disease one had pneumonia, one had chronic obstructive airways disease and one had severe underlying medical problems (hydrocephalus and quadriplegia) but there were two women who had a diagnosis of prolapse recorded and no other information.

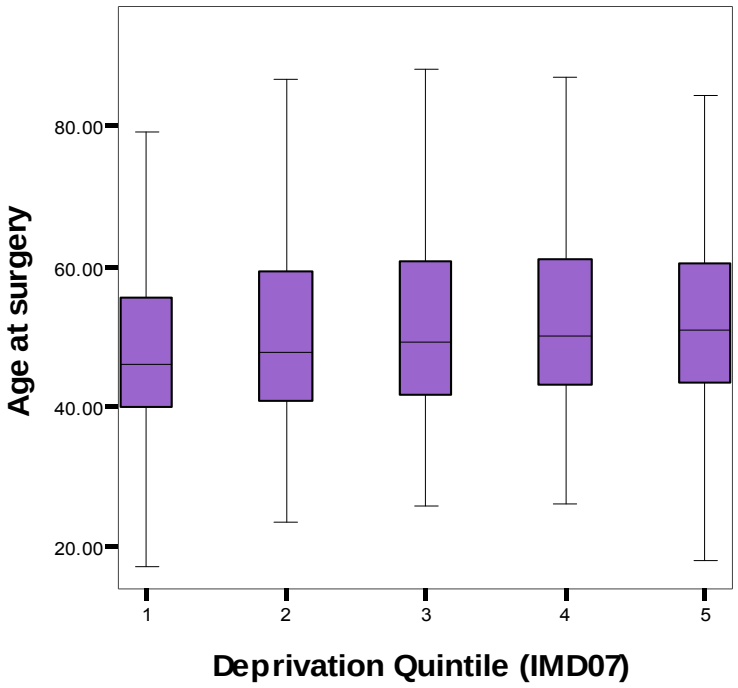
Thus five deaths in cases of benign disease gave an operative mortality of 5 in 5,090 or one per 1,000. For malignant disease it was 5 in 713, or seven per thousand. There were no deaths in cases of CIN.

6.1.9 Selected demographic factors for further description

6.1.9.1 Age at time of surgery compared with deprivation

Actual age at time of surgery was compared with IMD07 deprivation score; Spearman correlation = 0.129, $p<0.001$. Thus with increasing quintile (i.e. with decreasing deprivation) there was a small but significant increase in age at time of surgery, as demonstrated in the box plot at Figure 23.

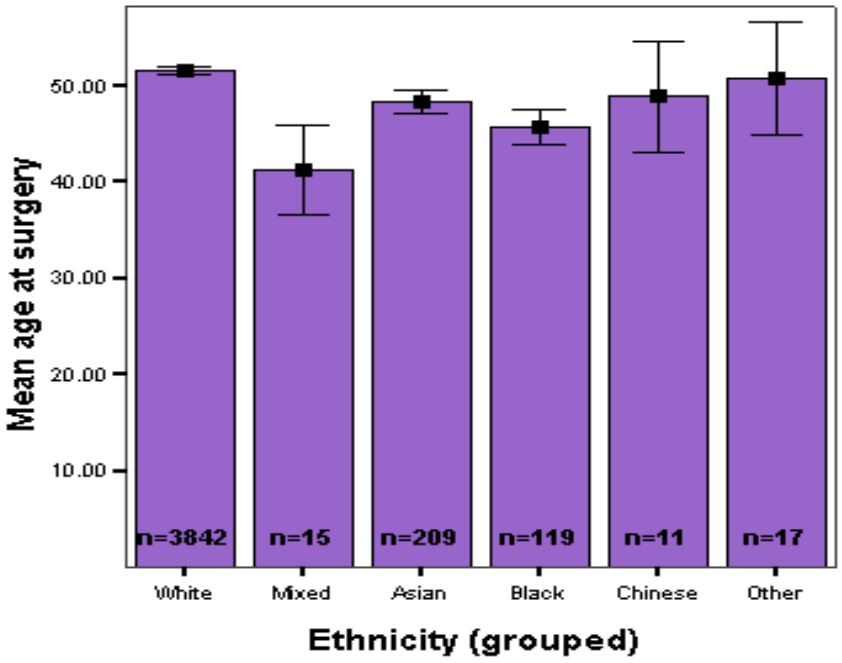
Figure 23. Age range for each deprivation quintile *(1 = most deprived))*



6.1.9.2 Age at time of surgery compared with ethnicity

Age was compared with ethnic grouping (6 groups: White, mixed, Asian, Black, Chinese, other stated) to look for an associations between increasing age and the various ethnic groups. The Kruskal-Wallis Test was used as the non-parametric alternative to a one way ANOVA: Kruskal-Wallis test statistic = 38.604 (5df, $p<0.001$), thus there was a highly significant association. The women of self declared 'Mixed and Black' ethnic origin were younger than the 'White' women, with 'Chinese', 'Other' and 'Asian' being in-between. This is illustrated in Figure 24.

Figure 24. Mean age of the various ethnic groups



Error bars represent 95% CI of mean

6.1.9.3 Duration of post operative stay compared with age at operation

Further to the observation in 6.1.7 that when classified into early, normal and delayed discharge, there were some differences between groups, the data were further explored to establish the validity of those findings: The duration of stay post operatively was compared with the age at time of surgery as it was predicted that older women may required a longer period of post operative recovery: Spearman correlation = 0.215, 2-tailed significance p=<0.001, thus a highly significant correlation exists with increasing age and increasing duration of stay. The analysis was repeated with just those women who remained in hospital for more than 6 days (N=872): Spearman = 0.153 p=<0.0001, a weaker correlation than with the more conventional duration of stay.

6.1.9.4 Duration of hospital stay compared with deprivation

Further to the observations in 6.1.7, the actual IMD07 (deprivation) score for each woman was compared with the actual duration of her post operative hospital stay: Spearman correlation = -0.026, p=0.042, a small negative correlation. Thus Kruskal Wallis test was then applied to the deprivation quintiles: χ^2=8.318 4df, p=0.081 which demonstrated that there were no meaningful differences between quintiles.

When those women whose post operative duration of stay was deemed to be 'normal' were excluded (up to 6 days) there was still no meaningful associations detected (Spearman correlation = -0.054, p=0.111).

6.1.10 Summary of section 6.1

This first section has examined the demographic details of the study population and has established that the crude and age standardised hysterectomy incidence is 23 per 10,000 women per annum in the West Midlands region. Surgery occurred at a median age of 48 years but with a wide range of 17 to 94 years. Thus, age specific incidence rates varied widely, with a peak of 63 per 10,000 women aged 45-49 years.

Hysterectomy incidence varied by ethnicity: hysterectomy was most commonly performed in Black women, having an incidence of 33 per 10,000 pa (assuming true study distribution of ethnicity in proportion to that provided). Ethnicity was recorded for 68.6% of the study population and all groups were represented.

Deprivation (IMD07) was also established to be associated with variability in incidence of hysterectomy: the most deprived quintile had an age standardised incidence of 25 per 10,000 compared with 20 per 10,000 in the least deprived. The West Midlands region is more deprived than the UK generally and thus although the study population was more deprived that the UK, compared to the regional data it was found to be very representative of women locally.

The study population had a mean and median of six cytology tests undertaken (range 0-31) including pre and post operative cytology. Duration of hospital stay varied from 0 to 81days but the median was 5. Ten women died during their admission, five of these had malignant disease (four were coded as having disseminated disease). Of the other five, three had co-morbidity. This gave a death rate of one per thousand for benign indications and seven per thousand for malignancy. A positive correlation was noted between increased age and increased duration of hospital stay.

There was also an association noted between increasing deprivation and decreasing age at time of surgery.

6.2 CERVICAL SCREENING HISTORY OF STUDY POPULATION: WHY DID THESE WOMEN NEED A HYSTERECTOMY OPERATION?

6.2.1 Cervical screening history overview

The personal screening records for the 6,141 participants were examined for trends: these varied from women never having any screening to a small number of women who underwent very intensive testing spanning several decades. Table 48 summarises the screening data which are then explored in more detail in the following sections:

Table 48. Description of collated cytology screening data

Variable	Results	Notes
Number of cervical cytology tests ever	36,151 tests in 6,141 women Range 0 - 31 tests Median = 6 IQR = 4 - 7 Skewness = 1.050 338 women never had any tests 23 women had 20 or more	A woman who completes full screening according to current guidelines (25-65yrs) would have approximately seven tests although 12 are possible in a woman who is fully compliant with screening recall dates and who does not have any pregnancies. Distribution skewed to the right.
Number of tests preoperatively	34,174 tests in 5,787 women Range 1 - 25 tests Median = 5 IQR = 4 - 7 Skewness = 0.920	Distribution mirrors that of total numbers of tests. 354 never had preoperative testing
Number of tests post hysterectomy	1,977 tests in 1,016 women, Range 1 - 10 tests Median = 1 IQR = 1 - 2 Skewness = 4.102	National guidelines concerning use of post operative cytology do not apply to women who had malignant disease, just benign or pre-invasive. Exponential decay in numbers. 16 only had post op testing.
Diagnosis at pre-op 'index' cervical cytology test	Normal or inadequate = 5,311 Dyskaryosis = 161 Invasive disease = 18 Borderline / other = 297 No test = 354	91.77% of index results normal or inadequate.

The group of women who never had any cervical cytology screening preoperatively was examined: these 354 women spanned the whole range of age, deprivation and ethnicity. There was no association detected between ethnicity and never having had cervical screening, this information was present for a similar proportion as the whole study (66.95%, *62.84 – 71.06* vs 68.6%, *67.63 – 69.57*). Age greater than 70 was associated with not being tested as anticipated because the national screening programme was only introduced in 1984,[15] Wilcoxon Z = -15.167 ($p<0.001$).

6.2.2 Summary of the index cervical cytology test

The final cervical screening test prior to hysterectomy was termed the 'Index' test and it is plausible that the result of this test had some bearing on the decision to undertake a hysterectomy operation. Thus, the index test was examined in some detail, whereas all the other screening tests that each woman underwent were summarised into an overall code for analysis.

6.2.2.1 Overview of index test result

Table 49 summarises the result of the index cervical screening tests for all the women: 83.8% were completely normal and only 2.7% were graded as inadequate, which is significantly below the national average for cervical screening prior to 2002.[28]

Table 49. The results of the final cytology test taken before surgery (the Index test)

Result of index test	Frequency	% *(CI)*
No preoperative test	354	5.76 *(5.27 – 6.25)*
Inadequate	165	2.69 *(2.35 – 3.03*)
Normal	5,146	83.80 *(83.03 – 84.57)*
Mild Dyskaryosis	43	0.70 *(0.52 – 0.88)*
Moderate Dyskaryosis	43	0.70 *(0.52 – 0.88)*
Severe Dyskaryosis	75	1.22 *(0.99 – 1.45)*
Severe, probable invasion	18	0.29 *(0.18 – 0.4)*
Glandular cells	52	0.85 *(0.66 – 1.04)*
Borderline changes only	129	2.10 *(1.80 – 2.40*)
Other	116	1.89 *(1.60 - 2.18)*
Total	***6,141***	***100.0***

6.2.2.2 Result of Index cervical cytology test compared with age

The result from the last test before surgery (4 bands, see Table 50) was compared with actual age at the time of surgery and confirmed that age was strongly associated with the index test result (Kruskall Wallis χ^2 =280.530 3df, p=<0.001). Thus women having a cancer diagnosis tended to be older than those having dyskaryosis.

Table 50. Index cervical cytology (4 groups) by mean age

Index test result	N	Mean age (yrs)	SD
Cancer	18	48.89	11.120
Dyskaryosis	161	43.54	10.466
Benign	5,146	50.35	12.088
Other	816	57.47	17.156
Total	***6,141***	***51.12***	***13.118***

This strong association was confirmed with the Kruskal Wallis test: χ^2 test statistic including 'other' group = 179.132, 3df (p <0.001) or excluding 'other' group Kruskal Wallis χ^2 = 56.599, 2df, p<0.001. Figure 25 illustrates this finding; although there is a lot of overlap in the age ranges for each result, the mean ages are clearly different.

Table 51 summarises the raw age data, broken into the 5-year age bands, for the Index test result and shows that the majority of women had normal index cytology results and these were mostly performed between the ages of 30 and 75 years. The most seriously abnormal findings were in women aged 30 to 70 years. There were very few abnormal test results from any women over the age of 70 years.

Figure 25. Age at surgery for various index cytology results

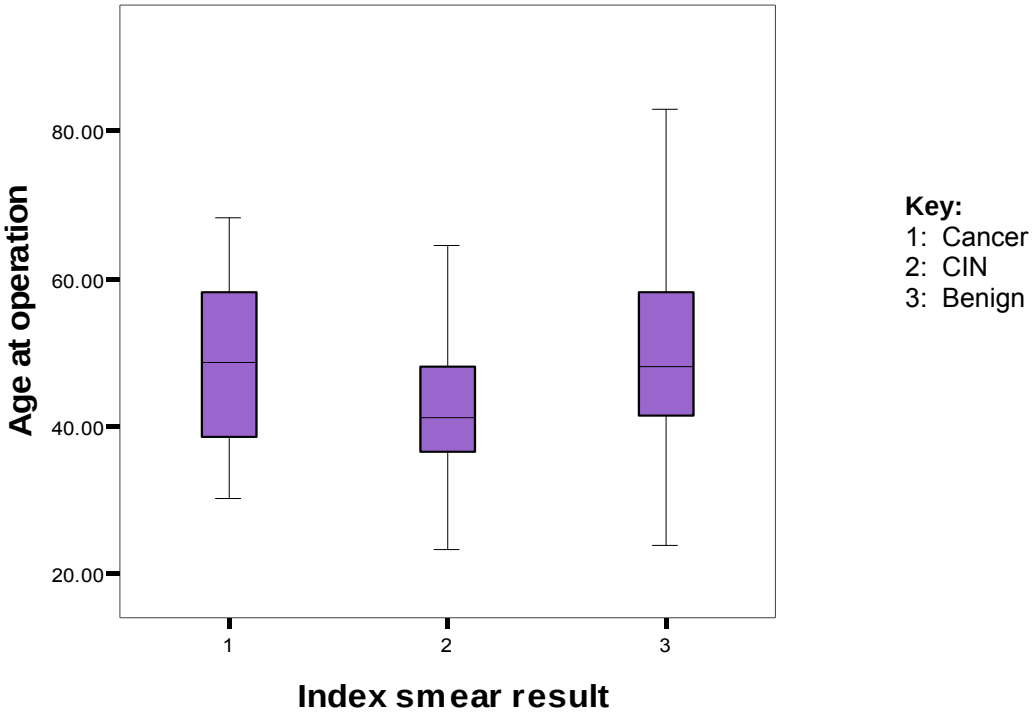


Table 51. 5 year age bands compared with result of index cytology test

	Result of Index cervical cytology test*										
	Cancer	**Dyskaryosis**			**Benign**	**Other**					**Total**
5 year bands	Invasive	Mild	Mod	Severe	Normal	Glandular	Borderline	Inad	N/K	No test	
<20	0	0	0	0	0	0	0	0	0	2	**2**
20-24.99	0	0	0	1	6	0	0	1	0	1	**9**
25-29.99	0	0	3	5	70	1	4	3	2	6	**94**
30-34.99	2	6	7	14	287	5	12	19	7	14	**373**
35-39.99	3	8	9	16	648	5	20	20	6	20	**755**
40-44.99	2	15	12	12	971	8	17	22	8	27	**1,094**
45-49.99	2	6	4	9	942	4	22	29	14	25	**1,057**
50-54.99	3	1	2	3	633	6	16	24	9	22	**719**
55-59.99	3	5	0	6	455	12	15	18	8	13	**535**
60-64.99	2	1	5	4	376	6	10	12	9	18	**443**
65-69.99	1	1	1	3	326	2	5	5	13	21	**378**
70-74.99	0	0	0	1	250	2	4	3	30	40	**330**
75-79.99	0	0	0	1	135	1	2	4	8	54	**205**
80-84.99	0	0	0	0	40	0	1	5	2	58	**106**
85-89.99	0	0	0	0	7	0	1	0	0	25	**33**
>90	0	0	0	0	0	0	0	0	0	8	**8**
Subtotal		*161*			*5,146*	*816*					
Total	***18***	***43***	***43***	***75***	***5,146***	***52***	***129***	***165***	***116***	***354***	***6,141***

** A full listing and explanation of all cytology results groups is given in table 14 in Chapter 5. The not known (N/K) group has been added where the given code was erroneous.*

6.2.2.3 Result of index test compared with deprivation score

When result of the Index test was compared with the deprivation quintile of the patient a significant difference was detected: Kruskal-Wallis χ^2 = 22.223 (1 df, p=<0.001), Table 52 includes these data.

It may be seen that with increasing affluence, the likelihood of the last cytology test before surgery being abnormal decreased and the likelihood of a normal test result increased. The association between deprivation and abnormal cervical screening has been established previously.[66]

Table 52. Index cervical cytology result by deprivation quintile

Quintile	Abnormal Index		Normal Index		Total
	N	% (CI)	N	% (CI)	
1. *Most Deprived*	75	5.44 (*4.43 – 6.45*)	1,303	94.56 (*93.55 – 95.57*)	1,378
2.	35	3.35 (*2.43 – 4.27*)	1,010	96.65 *(95.73 – 97.57*)	1,045
3.	27	2.38 (*1.64 – 3.12*)	1,107	97.62 (*96.88 – 98.36*)	1,134
4.	27	2.60 (*1.79 – 3.41*)	1,013	97.40 *(96.59 – 98.21*)	1,040
5. *Least Deprived*	15	2.06 (*1.19 – 2.93)*	713	97.94 (*97.07 – 98.81*)	728
Totals	**179**	**3.36** (*2.95 – 3.77*)	**5,146**	**96.64** (*96.23 – 97.05*)	**5,325**

6.2.2.4 Result of Index test compared with ethnic group

When results of the relevant index tests (i.e. excluding those who did not have an index or for whom their index test was of uncertain significance) were compared with ethnicity (6-group classification) of the patient, no meaningful difference was detected: Kruskal-Wallis χ^2 =5.224 (5 df, p=0.389), Table 53 summarises these data. As numbers of invasive disease detected at index test were so small it was inappropriate to draw conclusions.

Table 53. Index cytology test result by ethnicity

Ethnic group	Benign (%, *CI*)	Dyskaryosis	Invasive	*Total valid*	Other results	Total
White	3,242 (84.38, *82.23-85.53*)	89	11	*3,342*	500	**3,842**
Mixed	11 (73.33, *50.95-95.71*)	1	0	*12*	3	**15**
Asian	173 (82.78, *77.66-87.90*)	6	0	*179*	30	**209**
Black	95 (79.83, *72.62 – 87.04*)	4	1	*100*	19	**119**
Chinese	9 (81.82, *59.03-100*)	0	1	*10*	1	**11**
Other	11 (64.71, *41.99-87.43*)	1	0	*12*	5	**17**
Totals	**3,541** (84.05, *82.94-85.16*)	**101**	**13**	**3,655**	**558**	**4,213**

6.2.3 Summary of preoperative cervical screening history

6.2.3.1 Number of preoperative cervical screening tests compared with age

The number of cytology tests performed preoperatively was compared with each woman's' age and, as would be expected, there was a highly significant correlation noted: Spearman correlation = -0.216, $p<0.001$. However, that was a simplistic comparison which did not consider how many tests a woman would have been anticipated to have had, at any given age, assuming that all of her tests were normal and took place at approximately the correct time.

Thus an effort was made to predict how many cervical screening tests a woman should have undergone at any given age.

Until 2004, there was significant regional variation throughout the UK in terms of how often screening was occurring, despite the national screening programme being introduced in 1988 and ad-hoc screening occurring from the late 1960's, but the minimum stated target was one test every five years, from 20 - 65 years.[83] This provided an 'expected' minimum recommended figure for use as a baseline for comparisons and is based upon the screening guidelines that were in place in England prior to the changes introduced in 2004.[84]

Additionally, the estimates reflect the fact that older women may never have been offered the opportunity to be screened properly through their lifetime and very elderly ladies in particular would be expected to have had very few tests.

Table 54 summarises, what the authors suggests, are the realistically 'expected' minimum numbers of tests and these were applied for the purposes of analysis. This table also gives details of the observed numbers of cytology tests for the various age bands.

If current guidelines were applied rigorously (three yearly 25 – 50 years, five yearly until 65 years) then a woman could have up to 12 normal tests by the time she is aged 65. However, women often have gaps in their screening when pregnant or when relocating, additionally few have the discipline to book their routine follow-up exactly when it falls due, thus an 'expected minimum' was generated to serve as an educated approximation.

Table 54. Anticipated numbers of screening tests for each age band

Age band at surgery (2002-03)	Expected number of tests for age band	Number of women per band	Mean number of tests	Observed range	Observed total
<20	0	2	0	0	0
20-24.99	1	9	3.11	0 - 7	28
25-29.99	2	94	3.89	0 - 12	366
30-34.99	3	373	5.35	0 - 17	1,994
35-39.99	4	755	6.14	0 - 22	4,633
40-44.99	5	1,094	6.29	0 - 22	6,881
45-49.99	6	1,057	6.20	0 - 22	6,548
50-54.99	7	719	6.08	0 - 20	4,372
55-59.99	7	535	6.37	0 - 25	3,406
60-64.99	7	443	5.87	0 - 17	2,600
65-69.99	7	378	4.80	0 - 21	1,812
70-74.99	6	330	3.22	0 - 17	1,061
75-79.99	5	205	1.77	0 - 13	362
80-84.99	4	106	0.83	0 - 9	87
85-89.99	2	33	0.46	0 - 4	15
>90	1	8	0	0	0
Total	**-**	***6,141***	**-**	**-**	***34,165***

Table 55 summarises the anticipated numbers of women having each number of tests for the purposes of analysis.

Table 55. Expected minimum number of cervical cytology tests

Expected number of tests	Number of women	%
0	2	0.03
1	17	0.28
2	127	2.07
3	373	6.07
4	861	14.02
5	1,299	21.15
6	1,387	22.59
7	2,075	33.79
Total	***6,141***	***100.0***

The Wilcoxon rank sum test statistic, for paired observations, was applied to these data (the actual observed number of tests compared with the expected minimum), Z = -4.525, was highly statistically significant ($p<0.001$). This suggested that although the total 'realistically expected' number of tests was similar to the 'observed' total number i.e. total tests observed = 34,165, total expected = 34,176 (a difference of only 0.03%), the age distribution of these tests was significantly different.

Thus, women were having testing at a younger age than we had predicted. This is illustrated in Figure 26. This would imply that the study population (women having a hysterectomy) have different screening histories from women who do not require a hysterectomy.

Figure 26. Observed and expected numbers of preoperative cervical cytology tests

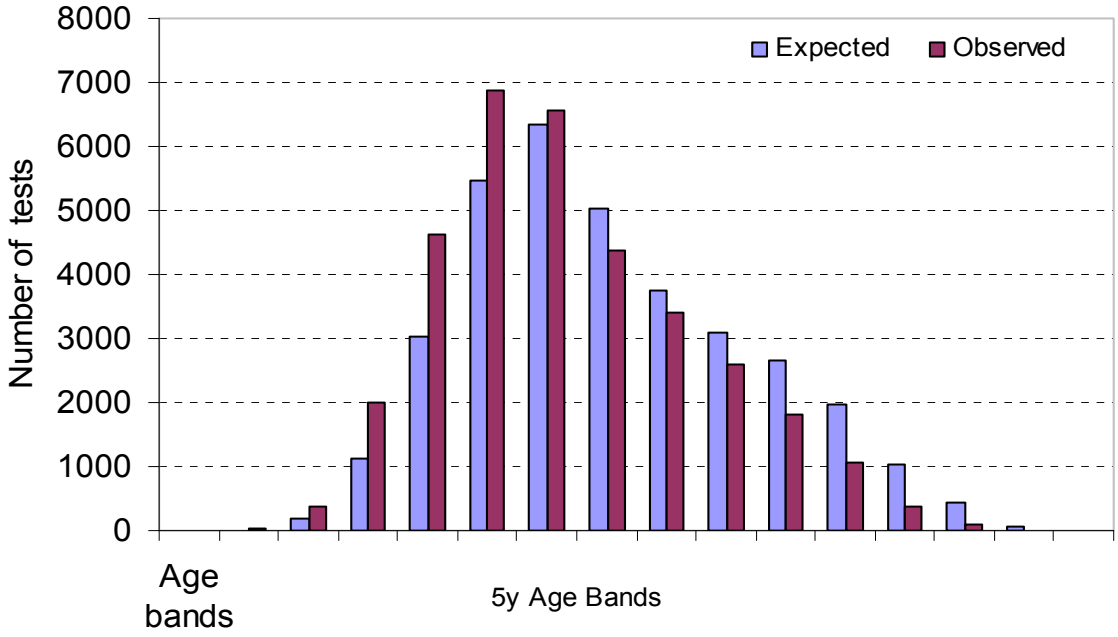
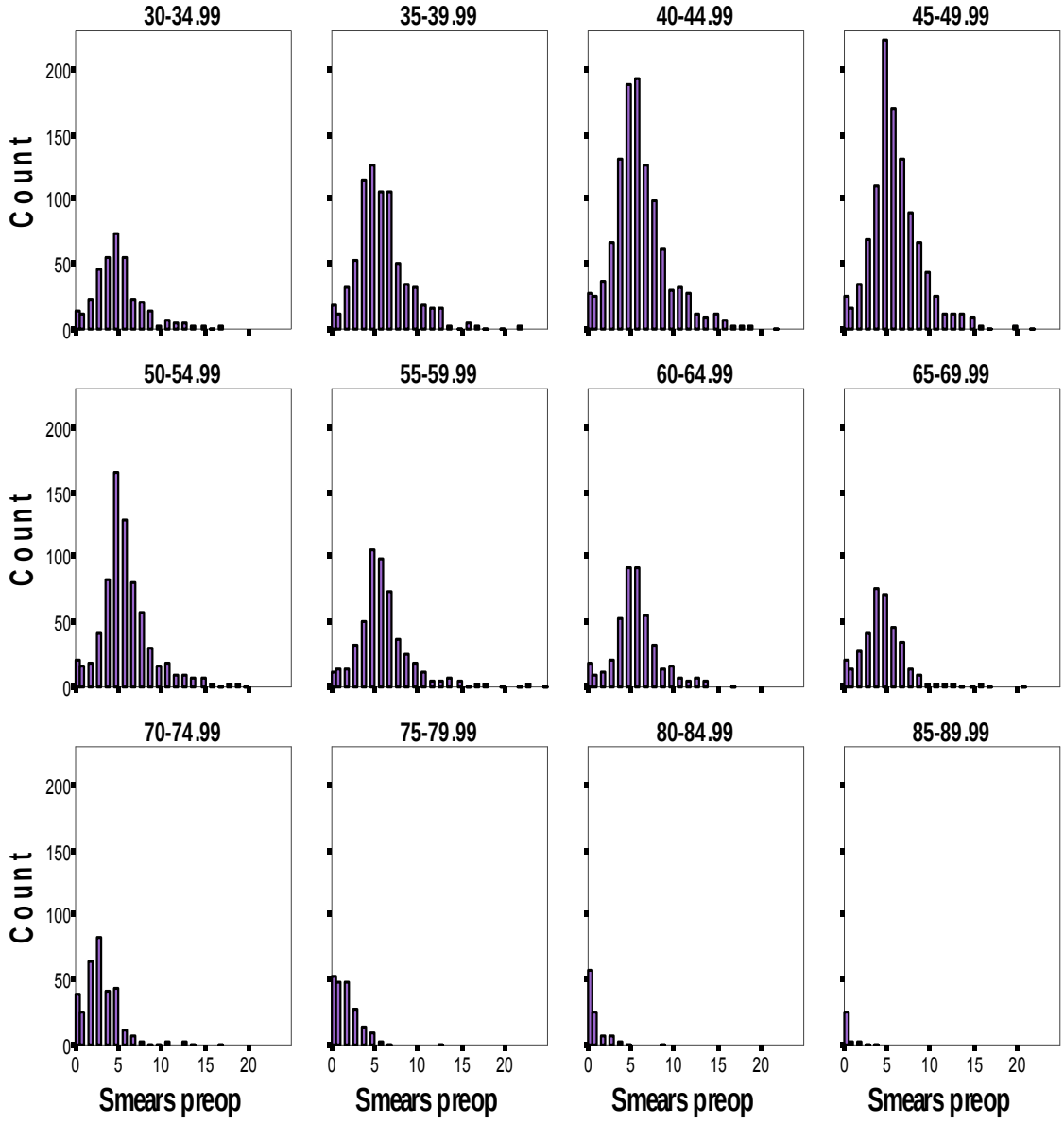


Figure 27 illustrates the numbers of women having cervical cytology tests preoperatively divided into five year age bands; the extreme ages were excluded as there were too few women to allow for meaningful comparisons. However, it can be seen that the profile of the histograms does vary as age increases, corresponding to the increase in number of tests according to the national screening programme but then tailing off in those women too old to have ever participated.

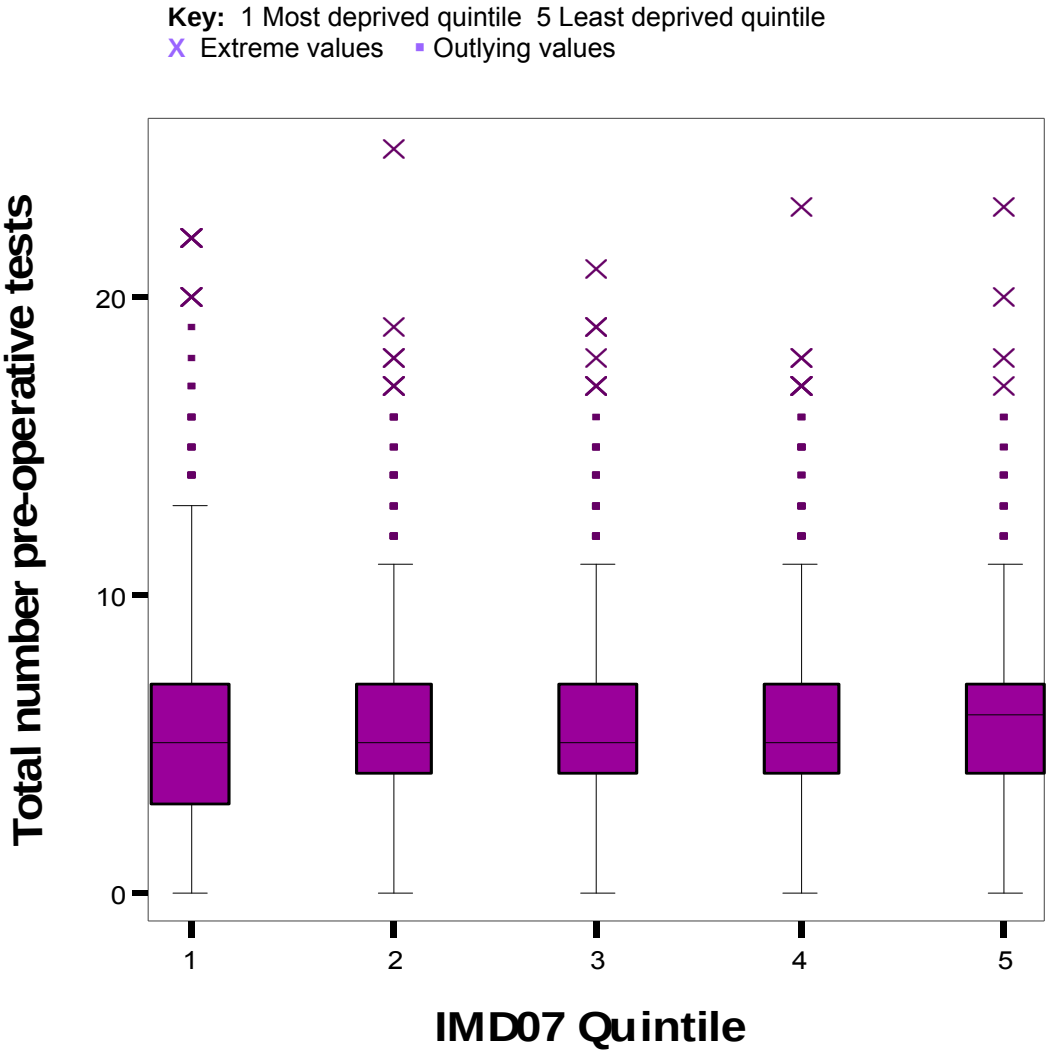
Figure 27. Number of screening tests preoperatively for various age bands



6.2.3.2 Number of preoperative screening tests compared with deprivation

A small negative correlation between the total number of screening tests preoperatively and the overall IMD07 deprivation score was established: Spearman coefficient = -0.058, ($p<0.001$), Figure 28. In view of the very small value, the importance of this observation in clinical practice is doubtful.

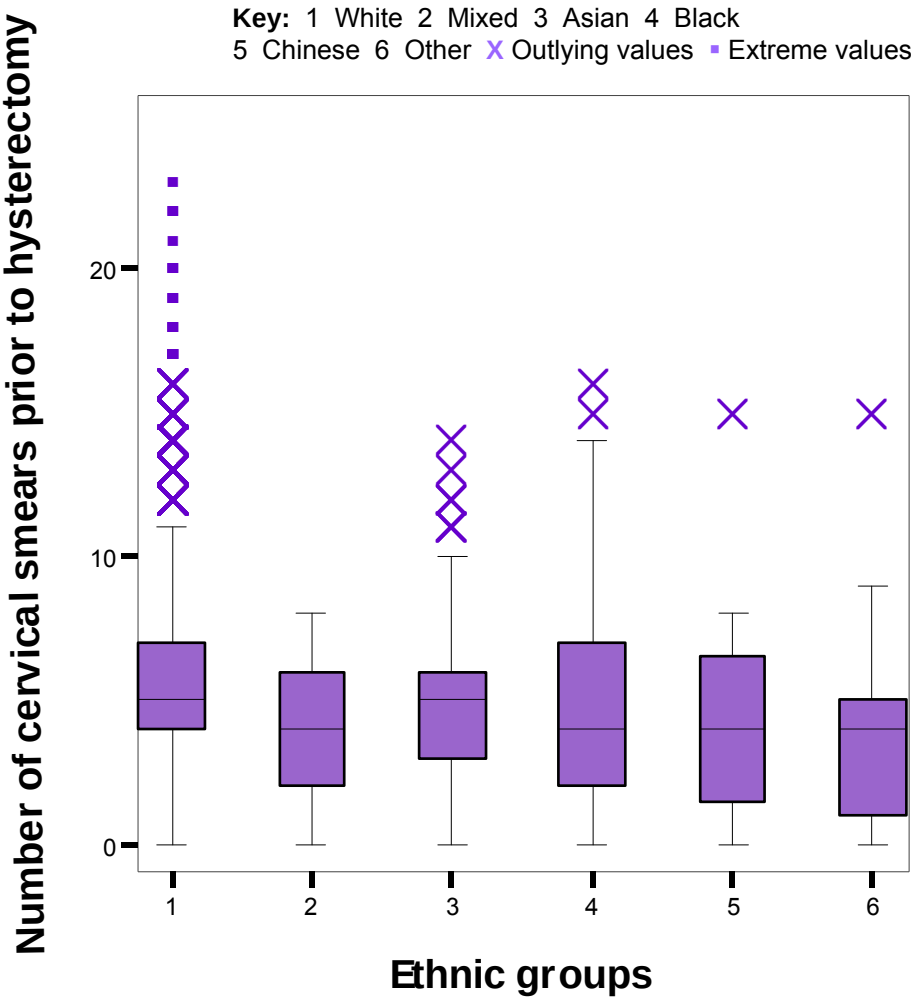
Figure 28. Number of preoperative screening tests, by deprivation quintile



6.2.3.3 Number of preoperative cervical screening tests compared with ethnicity

There was a significant association noted between ethnicity of the patients and the number of smears they had preoperatively: Kruskal Wallis test statistic = 30.053, (5df, p=<0.001). White women tended to have more screening tests than the other ethnic groups; in particular they had more tests than the mixed and Chinese groups as illustrated in Figure 29.

Figure 29. Ethnicity compared with number of preoperative cytology tests



6.2.4 WMCIU Screening Algorithm

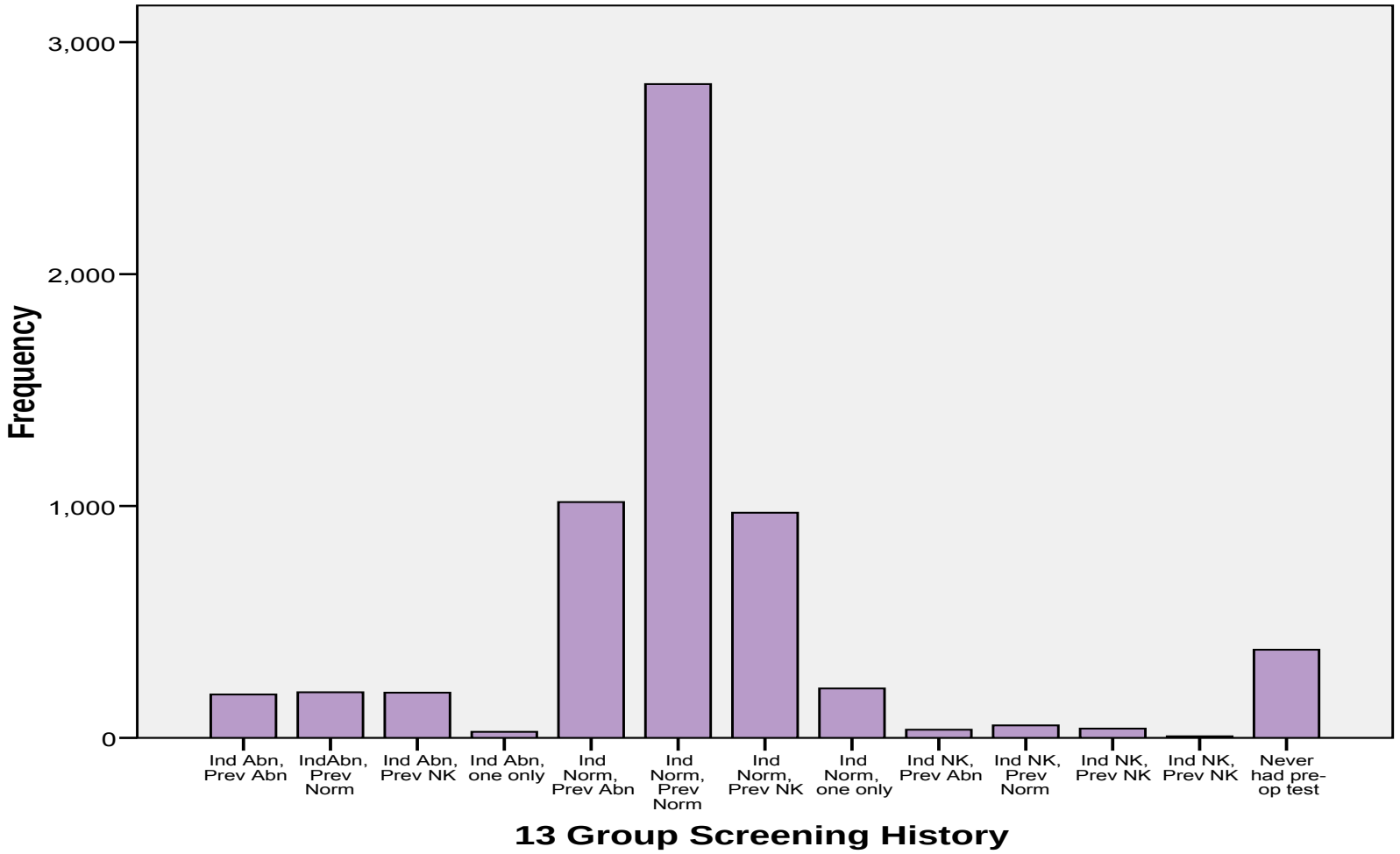
6.2.4.1 Overview of screening history

The data obtained from the screening coding algorithm was re-coded as described in Chapter 5 and summarised in Table 56 and Figure 30, allowing for sub-group comparisons. The algorithm coded as 'abnormal', results that were regarded as being of uncertain significance, thus the numbers differ slightly between the two sets of comparisons. Additionally the algorithm discarded any cytology undertaken in hospitals thus it applies to a smaller subset than the analysis on the raw data. In general numbers are sufficient to draw meaningful conclusions,.

Table 56. Groupings from WMCIU Screening algorithm - summary

Groups (four then 13 band groupings)	**N**	**%**	**95% CI**
1 - Index smear abnormal	605	9.85	9.22 – 10.48
2 - Index smear normal	5,020	81.75	80.94 – 82.56
3 - Index uncertain	136	2.21	1.90 – 2.52
4 - Never had a smear	380	6.19	5.68 – 6.70
	6,414	***100.00***	
11 - Index abnormal, previous abnormal	187	3.05	2.69 – 3.41
13 - Index abnormal, previous only normal	197	3.21	2.84 – 3.58
18 - Index abnormal, previous uncertain	195	3.18	2.81 – 3.55
19 - Index abnormal, no prior tests	26	0.42	0.28 – 0.56
31 - Index normal, previous abnormal	1,017	16.56	15.78 – 17.34
33 - Index normal, previous only normal	2,819	45.90	44.85 – 46.95
38 - Index normal, previous uncertain	971	15.81	15.04 – 16.58
39 - Index normal, no prior tests	213	3.47	3.09 – 3.85
81 - Index uncertain, previous abnormal	35	0.57	0.41 – 0.73
83 - Index uncertain, previous only normal	54	0.88	0.68 – 1.08
88 - Index uncertain, previous uncertain	40	0.65	0.48 – 0.82
89 - Index uncertain, no prior tests	7	0.11	0.04 – 0.18
99 - Never had preoperative testing	380	6.19	5.68 – 6.70
	6,141	***100.00***	

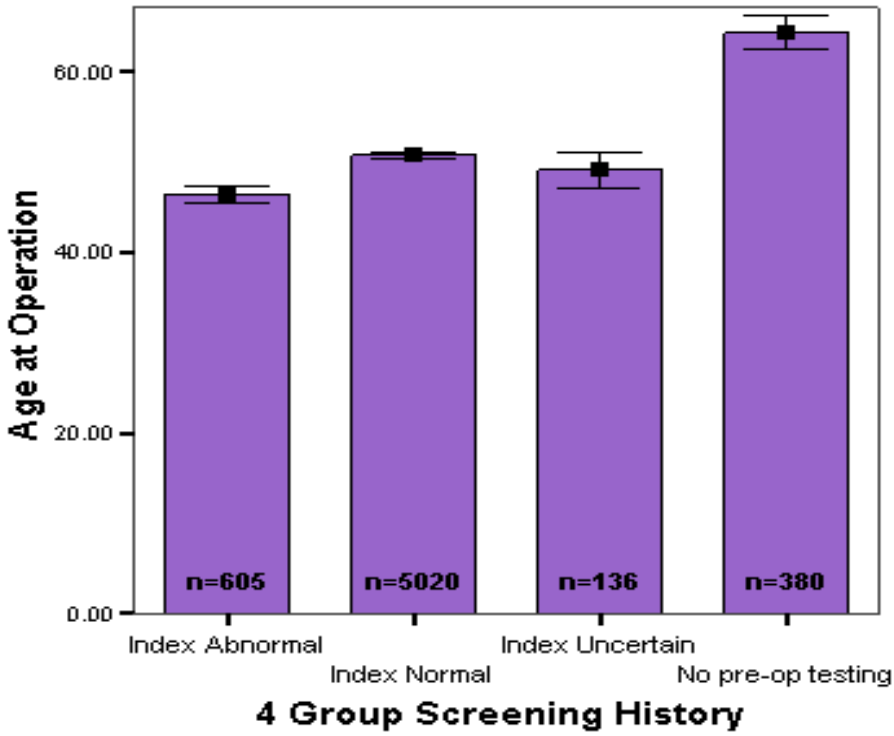
Figure 30. Frequencies of screening histories



6.2.4.2 Screening history compared with age at operation

Age was compared with the screening history groups from Table 56, to look for an association between increasing age and the various screening histories. The Kruskal-Wallis Test was used, as the non-parametric alternative to a one way ANOVA: Kruskal-Wallis test statistic for the 13-group banding = 436.747 (12df, $p<0.001$), Kruskal-Wallis test statistic for the 4-group banding = 287.961 (4df, $p<0.001$), thus there was a highly significant association, as illustrated in Figure 31, with those who never had any testing being older than those who had normal results and those with abnormal results being the youngest.

Figure 31. Screening History (4-group) compared with age at operation

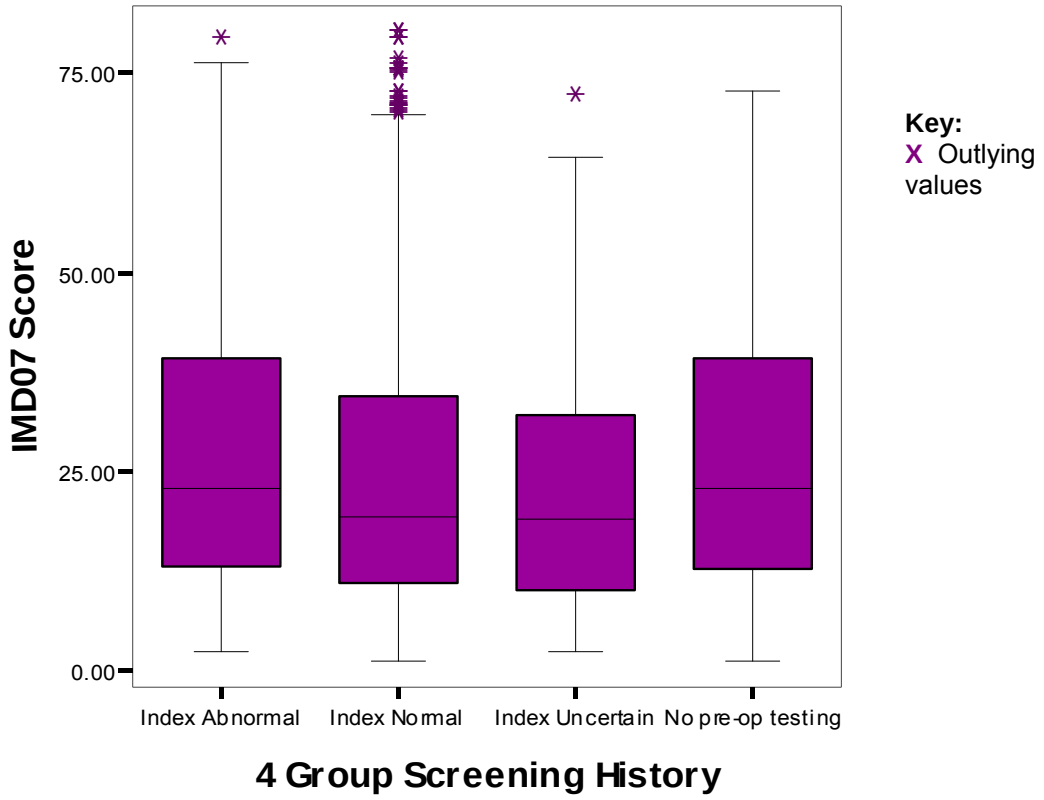


Error bars represent the 95% CI of the mean age at surgery

6.2.4.3 Screening history compared with deprivation score

Deprivation quintile and score were compared with the screening history groups, as in Table 56, to look for any association. Kruskal-Wallis test statistic for the 13-group banding = 43.037 (12df, $p<0.001$) and Kruskal-Wallis test statistic for the 4-group banding = 28.148 (3df, $p<0.001$), thus there was a significant association between absolute IMD07 score and overall screening history. This is illustrated in Figure 32 and demonstrates that those with abnormal index tests had a higher level of deprivation than those with normal test results. This is consistent with the findings previously presented in Table 52.

Figure 32. Deprivation scores of the screening history groups



6.2.4.4 Screening history compared with ethnicity

The screening history (4-group) was examined against the grouped ethnicity data where available, as summarised in Table 57. Then the proportions of women in each of the four bands were split into white or non-white to permit meaningful analysis and χ^2 was calculated: Pearson χ^2 (for the four groups in Table 57, based on the index result) = 5.785 (3df, p=0.1213) thus suggesting that there were no meaningful differences in screening history according to ethnic group.

Table 57. Ethnic groups and Index Screening test (algorithm)

4 Group Screening History	Ethnic group						
	White	Mixed	Asian	Black	Chinese	Other	Total
Index Abnormal	371	5*	18	12	1*	2*	409
Index Normal	3,160	8	177	89	8	11	3,453
Index Uncertain	89	0*	4*	3*	1*	1*	98
No preop testing	222	2*	10	15	1*	3*	253
Totals	***3,842***	***15***	***209***	***119***	***11***	***17***	***4,213***

** Many cells containing <5 expected frequency thus χ^2 not valid*

However, Table 58 includes the four and 13 group classifications of screening history and it may be seen that whilst some sub-groups had a proportion of White British women similar to the overall population, a few had quite different proportions.

Further comparisons were made to explore this observation: rather than consider the index test in isolation, the screening history prior to the index was explored (thus from Table 57 groups 11, 31, 81 were compared with groups 13, 33, 83). Pearson χ^2 = 6.373 (1df, p=0.012), thus suggesting that there may be some difference between these groups and that results from former screening history may also be associated with ethnicity.

Table 58. Screening history classifications and ethnicity

Groups (4 and 13 group classifications)	White	Non white	% White (CI)	Total
1 Index Abnormal	371	38	*90.71 (87.90 – 93.52)*	409
2 Index Normal	3,160	293	*91.51 (90.58 92.44)*	3,453
3 Index Uncertain	89	9	*90.82 (85.10 – 96.54)*	98
4 No pre-op testing	222	31	*87.75 (83.71 – 91.79)*	253
11 Index abnormal, previous abnormal	120	7	*94.49 (90.52 – 98.46)*	127
13 Index abnormal, previous only normal	128	11	*92.09 (87.60 – 96.58)*	139
18 Index abnormal, previous uncertain	111	17	*86.72 (80.84 – 92.60)*	128
19 Index abnormal, no prior tests	12	3	*80.00 (59.76 - 100)*	15
31 Index normal, previous abnormal	695	44	*94.05 (92.34 – 95.76)*	739
33 Index normal, previous only normal	1,753	160	*91.64 (90.4 – 92.88)*	1,913
38 Index normal, previous uncertain	586	67	*89.74 (87.41 – 92.07)*	653
39 Index normal, no prior tests	126	22	*85.14 (79.41 - 90.87)*	148
81 Index uncertain, previous abnormal	24	0	*100.00*	24
83 Index uncertain, previous only normal	36	5	*87.80 (77.78 – 97.82)*	41
88 Index uncertain, previous uncertain	24	3	*88.89 (77.04 – 100)*	27
89 Index uncertain, no prior tests	5	1	*83.33 (63.74 – 100)*	6
99 Never had pre-operative testing	222	31	*87.75 (83.71 – 91.79)*	253

When women who had only ever had an entirely normal screening (group 33), were compared with all other women who had undergone some screening there was no meaningful difference detected: Pearson χ^2=0.232 (1df, p=0.630). This is consistent with the earlier findings from the raw data (section 6.2.2.4).

6.2.5 Summary of section 6.2

This section has considered women's preoperative cervical screening. Of the 6,141 women, 5,787 (94.24%, 93.66 – 94.82) had some cervical screening (range 0 - 25 tests); those who did not have any were most likely to be aged over 70 years.

The last cervical screening test preoperatively, the 'index' test showed dyskaryosis or severe change in less than 3%, women with a more severe abnormality being older than those with dyskaryosis. There was an association with increasing deprivation and worsening test results, however there were no associations with ethnicity and index test results.

Overall screening histories of this population differ slightly from those of the general population in that they tended to have more tests performed at a younger age. White women had more screening than any other ethnic groups but coding of ethnicity was incomplete.

The application of the WMCIU algorithm, to code entire screening histories, permitted group comparisons and confirmed previous observations with respect to deprivation and age. When ethnicity was examined a mixed set of observations was generated; overall the test results suggested that ethnicity was not strongly related to having screening tests or to any particular pattern of results.

6.3 OUTCOME OF HYSTERECTOMY: WHAT WAS THE SURGICAL DIAGNOSIS?

6.3.1 Hospital site of surgery

6.3.1.1 Comparison between different hospitals

Section 5.2.2 summarised the raw data obtained from the various hospitals (before the small number of duplicate entries were removed), and identified a concern that three hospitals in the region, which were known to have active departments of obstetrics and gynaecology, did not have any hysterectomy operations attributed to them. However, there were noted to be missing or incomplete data on 712 women whose postcodes indicated that they would have been most likely to attend one of those three hospitals. This represented 11.59% (CI 10.79 – 12.39) of the data but because of uncertainty about allocating women to a hospital, particularly those near postcode boundaries, they were omitted from hospital based comparisons.

For the remaining hospitals, basic patient demographic factors were compared: median age at surgery, the proportion of women who were white, the median IMD07 deprivation score and the median post operative duration (Table 59). Also, because of the erratic ethnicity coding, the proportion of cases at each hospital that had their ethnicity coded was identified and the number of consultants at each site during the year was included.

Median age of hysterectomy did not differ greatly between hospitals (47 – 50 years). However, deprivation did vary widely across the region with median scores ranging from 9.2 to 43.7, illustrating the huge variability across the West Midlands. (IMD scores for individual patients ranged from 1.24 to 80.34, lower scores indicate less deprived areas, whereas lower ranks equate to greater deprivation).

Examining ethnicity coding illustrated clearly where some of the problems arose, with hospitals demonstrating a great variation in ethnicity coding; from 14% to 98% across the region. Of note, the hospital that recorded ethnicity accurately in less than 14% did not have any women coded as being 'white'. Closer examination revealed that almost 85% of the records were erroneously coded using the same classification consistently, which, on the basis of regional trends, is likely to represent white women.

The numbers of hysterectomies performed by, or under the care of, specific consultants varied widely; there were many instances of a consultant just having one or two cases in the year, but the nine most prolific surgeons were each responsible for over 100 hysterectomies. The most prolific was responsible for 189 cases, equating to almost four cases each week. The number of consultants at each hospital varied, as did the number of hysterectomy operations.

Table 59. Comparisons of hospital patient demographics

Hospital code	Number	% Total (*CI*) N=6,141	Median age (yrs)	Median deprivation (IMD07)	Ethnicity recorded in HES %	% White of those recorded	Median post op stay (days)	Number of clinicians
1	245	3.99 *(3.5 – 4.48)*	48.08	19.61	60.41	97.97	5	11
2	164	2.67 *(2.27 – 3.07)*	49.20	17.45	67.07	98.18	4	6
3	216	3.52 *(3.06 – 3.98)*	49.85	9.82	82.41	97.75	5	8
4	408	6.64 *(6.02 – 7.26)*	48.24	20.31	68.14	87.41	4	15
5	168	2.74 *(2.33 – 3.15)*	50.23	13.71	70.24	99.15	5	6
6	375	6.11 *(5.51 – 6.71)*	48.62	13.38	36.80	100.00	4	10
7	412	6.71 *(6.08 – 7.34)*	49.79	29.49	97.82	87.34	4	15
8	643	10.47 *(9.70 – 11.24)*	47.10	28.42	13.84	0	4	16
9	366	5.96 *(5.37 – 6.55)*	50.38	25.00	94.26	95.36	4	10
10	412	6.71 *(6.08 – 7.34)*	49.20	18.00	39.32	96.30	5	11
11	224	3.65 *(3.18 – 4.12)*	47.04	43.68	58.48	36.64	4	14
12	274	4.46 *(3.94 – 4.98)*	48.02	36.96	63.50	90.23	4	8
13	352	5.73 *(5.15 – 6.31)*	47.54	30.69	93.47	92.10	5	10
14	153	2.49 *(2.10 – 2.88)*	46.14	13.94	94.77	97.93	4	6
15	368	5.99 *(5.40 – 6.58)*	47.68	13.61	83.42	99.67	4	8
16	418	6.81 *(6.18 – 7.44)*	49.17	21.77	97.85	98.53	5	13
mis-coded	*943*	*15.36 (14.46 – 16.26)*	*48.58*	*17.47*	*79.43*	*96.13*	*5*	*46*
Population data	***6,141***	***100.00***	***48.38***	***24.59***	***68.60***	***91.19***	***5 days***	

6.3.1.2 Hospital based pathology data

As explained previously, the data obtained from some of the hospital histopathology departments could not be used to validate HES data as there were insurmountable difficulties linking hospital records to those from HES and comparing data from one hospital with another. This was substantially due to the fact that PIAG only permitted NHS number to be an identifier in this stage of the study and hospitals do not yet use this reliably and also because the laboratory coding was not consistent across sites.

Where linkage was attempted a poor match was obtained and thus no conclusions could reliably be drawn from this data source.

6.3.2 Operative procedures undertaken (OPCS4 codes)

6.3.2.1 Overview of OPCS4 surgical procedure codes

There were up to nine procedures listed per patient, with the majority of patients having at least two. These were grouped into seven main sections to facilitate analysis. Table 60 summarises these data.

Reassuringly, every woman had a 'gynaecological surgery' code recorded at least once in her data (i.e. their hysterectomy operation code, which was one of the inclusion criteria for the data from HES), thus even those who had abdominal or breast surgery also underwent a gynaecological operation.

When blank, invalid or unhelpful codes were excluded, the range of useful codes was from one to nine per woman, with most having two. Almost 86% of codes were gynaecological, 11% related to abdominal surgery with 3% concerning bladder or genitourinary surgery.

Table 60. Collated OPCS codes

Meaning of grouped OPCS codes	Diag 1	Diag 2	Diag 3	Diag 4	Diag 5	Diag 6 - 9	Total codes	% of all codes *CI*
Breast surgery	2	1	6	2	0	0	**11**	0.08 *0.03 – 0.13*
Abdominal or GI tract surgery	169	111	709	334	62	23	**1,408**	10.80 *10.27 – 11.33*
Genito-urinary or bladder surgery	22	64	202	88	17	8	**401**	3.08 *2.78 – 3.38*
Vaginal or prolapse surgery	675	354	75	21	2	3	**1,130**	8.67 *8.19 – 9.15*
Gynaecological surgery	5,253	4,369	336	77	16	6	**10,057**	77.14 *76.42 – 77.86*
Obstetric surgery	20	3	3	4	1	0	**31**	0.24 *0.16 – 0.32*
Other codes or blank cells	0	1,239	4,810	5,615	6,043	24,524	42,231	N/A
Total of useful codes (1-6)	***6,141***	***4,902***	***1,331***	***526***	***98***	***40***	***13,038***	***100***

6.3.2.2 Operation sub-type demographics

The gynaecological surgery codes were then examined to establish what type of hysterectomy procedure had been undertaken i.e. a sub-total or total operation. In a few cases it was impossible to distinguish the operation type from the OPCS code and so an 'unknown' group was also created. Table 61 summarises the key demographic comparisons between these three groups.

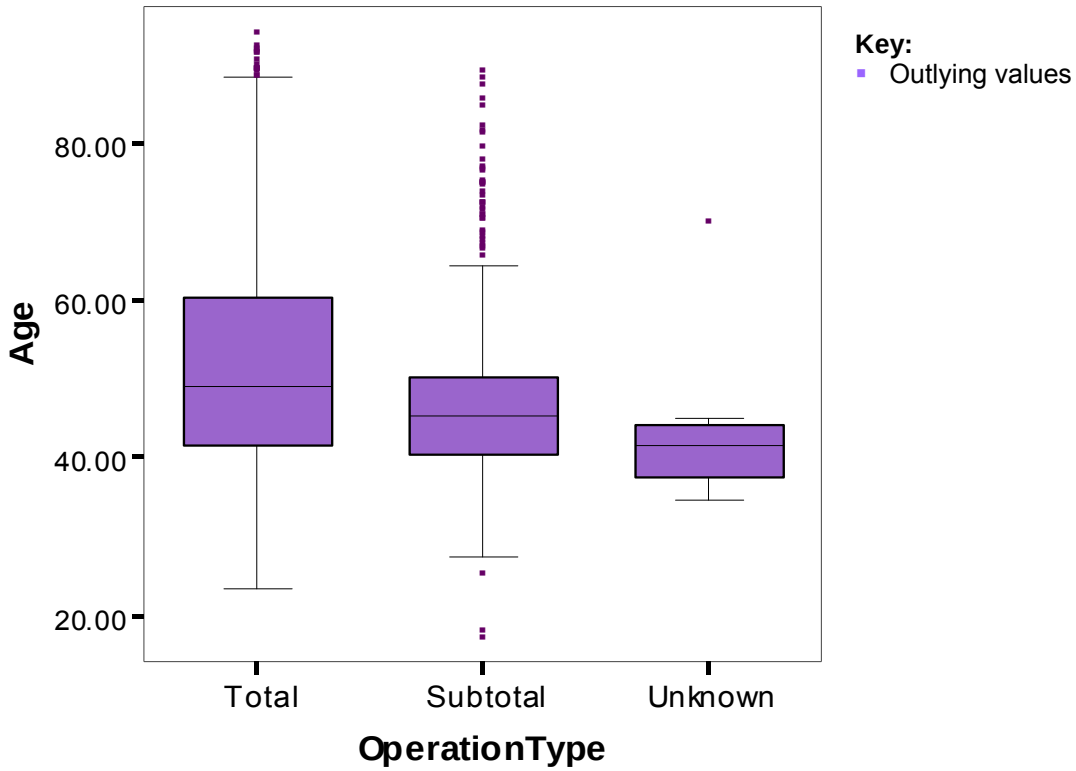
Table 61. Summary of differences in demographic data between hysterectomy sub-types

Comparator *whole study population* *N = 6,141*	**Total Hysterectomy** **N = 5,697** % = 92.77	**Sub total Hysterectomy** **N = 436** % = 7.10	**Unknown** **N = 8** % = 0.13	**Statistical test**	**Notes**
Age (6,141) *Mean = 51.52* *Median = 48.38* *Skewness = 0.606* *IQR = 18.21*	Mean = 51.44 Median = 48.88 Skewness = 0.562 IQR= 18.76	Mean = 47.01 Median = 45.166 Skewness = 1.267 IQR= 9.68	Mean = 43.79 Median = 41.409 Skewness = 2.247 IQR= 8.01	Kruskal Wallis χ^2=52.055, 2df, p<0.001	Thus there is a significant difference in age between the three subgroups with women having a total hysterectomy being somewhat older than the other two groups. See Figure, below.
Deprivation (6,141) *Overall Mean = 24.59* *Median = 19.70* *Skewness =0.847* *IQR = 23.94*	Mean = 24.472 Median = 19.640 Skewness = 0.850 IQR= 23.61	Mean = 26.217 Median = 20.490 Skewness = 0.780 IQR=27.56	Mean = 22.33 Median = 18.84 Skewness = 0.587 IQR= 30.73	Kruskal Wallis χ^2=2.502 2df, p=0.286	There was no association established between operation type and deprivation score, either absolute or in quintiles. See Figure.
<u>Quintiles (N/%)</u> *1 1,628 / 26.51%* *2 1,210 / 19.70%* *3 1,295 / 21.09%* *4 1,177 / 19.17%* *5 831 / 13.53%*	 1,490 / 91.52% 1,139 / 94.13% 1,205 / 93.05% 1,086 / 92.27% 777 / 93.50%	 136 / 8.35% 70 / 5.79% 88 / 6.80% 90 / 7.655 52 / 6.26%	 2 / 0.12% 1 / 0.08% 2 / 0.15% 1 / 0.08% 2 / 0.24%	 Pearson χ^2 = 9.891 8df p=0.273 (5cells count less than 5)	 Excluding unknown from the χ^2 analysis confirms that there is no association detected between deprivation and operation type (Pearson χ^2 = 8.649, 4df p=0.070).
Ethnicity (4,213) *White: 3,842 / 91.19%* *Mixed: 15 / 0.365%* *Asian: 209 / 4.96%* *Black: 119 / 2.82%* *Chinese: 11 / 0.26%* *Other: 17 / 0.40%*	% 3,583 / 93.26% 13 / 86.67% 196 / 93.78% 102 / 85.71% 8 / 72.73% 16 / 94.12%	% 254 / 6.61% 2 / 13.33% 13 / 6.22% 17 / 14.29% 3 / 27.27% 1 / 5.88%	% 5 / 0.13% 0 0 0 0 0	Pearson χ^2 = 18.846 5df p=0.002 (3cells count less than 5)	Thus there is an association between ethnicity and operation type. Including 'unknown' in the analysis gave Pearson χ^2 = 19.351, 10df p=0.036 but 9 cells count less than 5.
Duration of post op stay (6,136) *Median = 5 days* *Skewness = 6.781* *IQR = 4 - 5* *Range = 0 - 81*	Median = 5 Skewness = 6.969 IQR= 1 Range = 0 - 81	Median = 5 Skewness = 4.225 IQR= 2 Range = 0 - 31	Median = 6 Skewness = 2.412 IQR= 6 Range = 4 - 29	Kruskal Wallis χ^2=5.966 2df, p=0.051	Thus no association between duration of post operative stay and type or operation. Analysis excluding the 'unknown' group confirms this: Kruskal Wallis χ^2=1.391 1df, p=0.238.

It may be seen that only eight women could not have their operation type established and 7.10% (n=436, CI 6.46 – 7.74) of women had a subtotal hysterectomy.

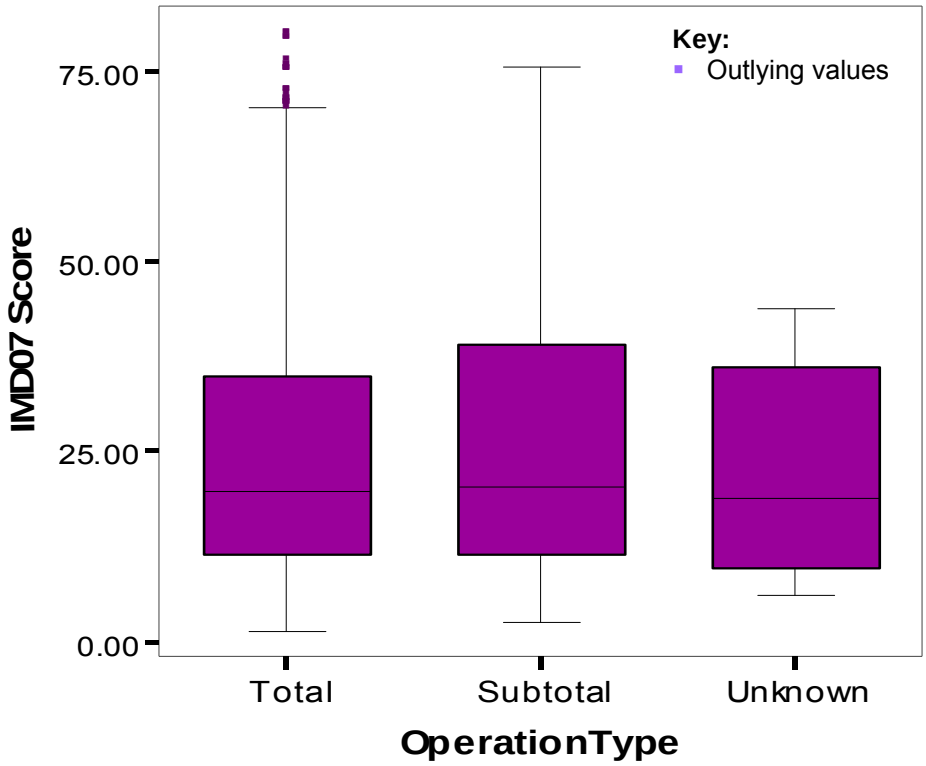
The three groups differed in two main ways. Firstly those women undergoing a sub total hysterectomy were younger than those having a total hysterectomy (Figure 33), with the unknown group being even younger. Also in terms of their ethnicity (where stated) white women were more likely to have total hysterectomies when compared to black and Chinese women although numbers were very small.

Figure 33. Age at surgery compared with operation type



In terms of deprivation (Figure 34) and duration of stay post operatively, the three groups did not differ significantly, with total and subtotal surgery having a medial post operative duration of 5 days. Considering women who were discharged within two days of surgery, no difference was found in the proportions having a total or other variant of hysterectomy.

Figure 34. Deprivation score compared with operation type



6.3.3 Diagnosis at time of operation

6.3.3.1 Overview of operative diagnosis

Each woman had between one and eleven valid ICD10 diagnostic codes recorded; each code was allocated to a group to allow for meaningful analysis (Table 62). There were over 11,000 codes in total; almost 20% were of no interest but 6% related directly to a gynaecological malignancy.

Table 62. Collated, grouped ICD10 codes

Meaning of diagnosis codes	Number (total)	% of all codes	*CI*
No interest to project	1,168	10.28	*9.72 – 10.84*
Neoplasm, malignant, non gynae	143	1.26	*1.05 – 1.45*
Neoplasm, in-situ, non gynae	3	0.03	*0 – 0.06*
Neoplasm, benign, non gynae	22	0.19	*0.11 – 0.27*
Obstetric general	82	0.72	*0.56 – 0.88*
Neoplasm, malignant gynae	676	5.95	*5.52 – 6.38*
Neoplasm, in-situ, gynae	94	0.83	*0.66 – 1.00*
Neoplasm, intraepithelial neoplasia, gynae	76	0.67	*0.52 – 0.82*
Neoplasm, benign & unknown, gynae	1,902	16.74	*16.05 – 17.43*
Other gynae diagnoses: inflammation	407	3.58	*3.24 – 3.92*
Other gynae diagnoses: infection	0	0	*0*
Other gynae diagnoses: bleeding, menstrual, menopausal	2,400	21.12	*15.46 – 18.46*
Other gynae diagnoses: NOS, endometriosis, prolapse, infertility, polyp, miscarriage	3,339	29.39	*28.55 – 30.23*
Descriptive terms only (not true diagnosis), non gynae	1,049	9.23	*8.70 – 9.76*
Total number of codes	***11,361***	***100***	

The 'worst' of all diagnoses was established, for each woman, by use of a basic ranking where, any malignancy was coded as being worst, then any intraepithelial neoplasia or carcinoma in-situ, followed by any benign disease and finally a selection of other codes that were not diagnostic were regarded as unclassifiable.

Next, the regional raw screening data for the result of the last cervical screening test prior to hysterectomy (index) was considered: if this took place within six months (180 days) of the operation then the diagnosis was regarded as being related to surgery and so that if serious cervical pathology was detected which was worse than the main diagnosis then the woman was classified to a more serious group. This reclassification was justified because it is possible for colposcopic treatment to remove all trace of CIN or in-situ disease but be severe enough for hysterectomy to be recommended, particularly if the patient has completed her family.

Table 63. Final 'worst diagnosis' per study participant classification

Code	Explanation	N	%	*CI*
1	Cancer or Malignancy	713	11.61	*10.81 – 12.41*
2	Intraepithelial neoplasia or carcinoma in-situ	184	3.00	*2.57 – 3.43*
3	Benign disease	5,090	82.89	*81.95 – 83.83*
9	Unclassifiable	154	2.51	*2.12 – 2.90*
	Total	***6,141***	***100***	

The final 'worst diagnosis' (Table 63) was a combination of the worst of each woman's recorded ICD10 codes and, if applicable, her cervical screening within six month of surgery. In reality in only 28 cases did the screening result change the outcome (four from CIN to malignant, sixteen from benign to CIN, three from unclassifiable to CIN and five cases from unclassifiable to benign diagnosis).

6.3.3.2 Operative diagnosis: description of group demographics

The three main diagnosis groups (benign, intraepithelial neoplasia and malignancy) were compared in terms of age, deprivation, ethnicity and duration of post operative stay. Table 64 summarises the key demographic differences. It may be seen that there was a significant association between age and diagnosis; Kruskal Wallis test statistic = 546.441, a large and highly significant result (2df, $p<0.001$). Thus, women with malignant disease were significantly older than the other groups of women. However there were no associations detected with respect to diagnosis and deprivation, (quintiles or raw data).

Ethnicity was compared and demonstrated an association between being of White ethnicity and having a worse final diagnosis i.e. being non-white is associated with an increased likelihood of having a benign diagnosis, Pearson χ^2=17.863 (2df, $p<0.001$). Duration of post operative stay was examined and results confirmed that having a cancer diagnosis was positively associated with a longer duration of hospital admission, Kruskal Wallis = 428.010 (2df, p=<0.001). However, even some of these cases were discharged within two days of surgery (n=25 or 6.6% of the women discharged very early).

Table 64. Demographic summary worst diagnosis at hysterectomy

Comparator *whole study population* *N = 6,141*	**Cancer / malignancy** **N = 713** % = 11.61	**Intraepithelial neoplasia** **N = 184** % = 3.00	**Benign** **N = 5,090** % = 82.90	**Statistical test**	**Notes** (Unclassifiable = 154 or 2.51%)
Age (6,141) *Mean = 51.52* *Median = 48.38* *Skewness = 0.606* *IQR = 18.21*	Mean = 62.106 Median = 62.776 Skewness = -0.396 IQR= 17.15	Mean = 45.549 Median = 42.800 Skewness = 0.795 IQR= 16.82	Mean = 49.852 Median = 47.288 Skewness = 0.752 IQR= 15.66	Kruskal Wallis χ^2=546.441 2df, p= <0.001	Thus a significant association exists with women having a cancer diagnosis generally being older than women in the other groups.
Deprivation (6,141) *Overall Mean = 24.59* *Median = 19.70* *Skewness =0.847* *IQR = 23.94*	Mean = 23.716 Median = 18.620 Skewness = 0.959 IQR= 22.92	Mean = 26.550 Median = 23.050 Skewness = 0.649 IQR= 24.71	Mean = 24.597 Median = 19.650 Skewness = 0.839 IQR= 24.13	Kruskal Wallis χ^2=5.508 2df, p=0.064	There was no important association established with diagnosis and deprivation.
<u>Quintiles (N/%)</u> *1 1,628 / 26.51%* *2 1,210 / 19.70%* *3 1,295 / 21.09%* *4 1,177 / 19.17%* *5 831 / 13.53%*	 175 / 11.04% 137 / 11.63% 153 / 12.11% 145 / 12.63% 103 / 12.63%	 56 / 3.54% 45 / 3.82% 37 / 2.93% 28 / 2.43% 18 / 2.21%	 1,353 / 85.29% 995 / 84.53% 1,073 / 84.96% 975 / 84.93% 694 / 85.15%	Pearson χ^2 = 8.858 8 df p=0.354 (0 cells less than 5)	The analysis of quintiles rather than crude IMD07 score confirms that there is no strong association between deprivation and diagnosis.
Ethnicity (4,213) *White: 3,842 / 91.19%* *Mixed: 15 / 0.365%* *Asian: 209 / 4.96%* *Black: 119 / 2.82%* *Chinese: 11 / 0.26%* *Other: 17 / 0.40%*	% 492 / 13.06% 2 / 13.33% 12 / 5.91% 4 / 3.48% 2 / 25.00% 2 / 12.50%	% 110 / 2.92% 0 / 0% 4 / 1.97% 0 / 0% 0 / 0% 1 / 6.25%	% 3,166 / 84.02% 13 / 86.67% 187 / 92.12% 111 / 96.52% 6 / 75.00% 13 / 81.25%	Pearson χ^2 = 25.320 10 df p=0.005 (7 cells count less than 5)	There appeared to be an association between ethnicity and diagnosis but small numbers made interpretation difficult. However, when the ethnicity was split into just 'white' or 'non white' there were no low values and Pearson χ^2 = 17.863 2 df p=<0.001, highly significant.
Duration of post op stay (6,136) *Median = 5 days* *Skewness = 6.781* *IQR = 4 - 5* *Range = 0 - 81*	Median = 6 Skewness = 3.716 IQR = 3 Range = 0 - 50	Median = 4 Skewness=11.316 IQR = 1 Range = 0 - 81	Median = 4 Skewness = 4.560 IQR = 1 Range = 0 - 42	Kruskal Wallis χ^2= 428.010 2df, p= <0.001	Thus women having the worse diagnosis tended to have a longer post operative stay overall.

6.3.3.3 Operative diagnosis compared with index cervical cytology result

The most recent test before surgery (the index test) was compared with result at hysterectomy; there was a positive association between the two, with comparable results, highlighted in Table 65, giving a highly significant Pearson χ^2=1,612.528 (9df, p<0.001). It must be noted that a cytology result of dyskaryosis is not the same as a histo-pathological diagnosis of CIN (see Chapter two, section 2.2.1 for full explanation).

Table 65. Worst diagnosis compared with index cervical cytology test

		Index smear result				
		Probable invasion	Dyskaryosis (mild - severe)	Normal	Unclassifiable	**Totals**
Hysterectomy	Cancer/Malignant	13	25	487	188	**713**
	CIN/ In situ	3	83	67	31	**184**
	Benign	2	42	4,471	575	**5,090**
	Unclassifiable	0	11	121	22	**154**
	Totals	***18***	***161***	***5,146***	***816***	***6,141***

The index result was then grouped into two basic blocks of normal or abnormal (including all dyskaryosis and invasive results); this was then compared with the worst diagnosis at surgery (split into normal or abnormal). It had been postulated that these results would be strongly related with an abnormal index test providing a good predictor of an abnormal result at hysterectomy, however, this proved not to be the case: McNemar test for equal proportions = 433.246, p=<0.001, Table 66, thus although there was an association, there is still substantial disagreement.

Table 66. Comparison of Index cytology result with hysterectomy diagnosis

Index result	Abnormal hysterectomy	Normal hysterectomy	Total
Index abnormal	124	44	168
Index normal	554	4,71	5,025
Total	***678***	***4,515***	***5,193***

6.3.3.4 Operative diagnosis compared with preoperative screening history

Having compared the index screening test, the main operation results groups were compared against the full cervical screening histories (from the WMCIU algorithm, section 6.2.4) to establish if there were any associations. The algorithm coding had generated 13 groups (Table 56), however, those where the index test was uncertain were excluded from the analysis as numbers were so small and thus nine groups were compared, see Table 67.

A cross tabulation of these data was performed and Pearson χ^2=622.485 (16df, p=<0.001) thus suggesting that there are important differences between the various groups. The Kruskall Wallis test was applied to the three diagnosis groups in each of the nine categories in Table 67 and again confirmed a significant association with the test statistic χ^2=248.073 (8df, p=<0.001). Women who had never been tested or had only had one test preoperatively were more likely to have a cancer diagnosis than the other groups, whereas for CIN the key factor was having had several abnormal tests.

Table 67. Cervical screening entire history code compared with operative diagnosis

Screening history	**Cancer N**	***Cancer % CI***	**CIN N /**	***CIN % CI***	**Benign N**	***Benign % CI***	**Total**
Index abn, prev abn	25	*14.12 8.99-19.25*	41	*23.16 16.95-29.37*	111	*62.71 55.59-69.83*	177
Index abn, prev normal	30	*15.79 10.60-20.98*	21	*11.05 6.59-15.51*	139	*73.16 66.85-79.46*	190
Index abn, pre unknown	20	*10.75 6.30-15.20*	29	*15.59 10.38-20.80*	137	*73.66 67.33-79.99*	186
Index abn, only one test	6	*24.0 7.26-40.74*	5	*20.00 4.32-35.68*	14	*56.0 36.54-75.46*	25
Index normal, prev abn	97	*9.80 7.95-11.65*	23	*2.32 1.38-3.26*	870	*87.88 85.85-89.91*	990
Index normal, prev normal	304	*10.99 9.82-12.16*	29	*1.05 0.67-1.43*	2,433	*87.96 86.75-89.17*	2,766
Index normal, unknown	65	*6.90 5.28-8.52*	11	*1.17 0.48-1.86*	866	*91.93 90.19-93.67*	942
Index normal, one test only	48	*22.75 17.09-28.41*	7	*3.32 0.90-5.74*	156	*73.93 68.01-79.85*	211
Never tested	100	*27.47 22.88-32.06*	8	*2.20 0.69-3.71*	256	*70.33 65.64-75.02*	364
Totals	***695***	***11.88***	***174***	***2.97***	***4,982***	***85.15***	***5,851***

6.3.3.5 Operative diagnosis compared with type of operation

The worst diagnosis at surgery was compared with type of operation (total hysterectomy or 'other') as it was postulated that women with a diagnosis of cancer would be more likely to undergo a total hysterectomy. A cross tabulation of the data (Table 68) gave a Pearson χ^2=16.458 (2df, p=<0.001), a result suggesting that there may be differences in operation type between the groups.

The Kruskall Wallis test was then applied to the three diagnosis groups however a significant association was not established this time with the test statistic χ^2=15.292 (2df, p=0.54). Thus women who had a diagnosis of cancer or CIN were not particularly more likely to undergo a total hysterectomy rather than a subtotal variant.

Table 68. Hysterectomy type compared with operative diagnosis

Operation type	Cancer	% CI	CIN	% CI	Benign	% CI	Total
Total hysterectomy	678	*12.21 11.35-13.07*	181	*3.26 2.79-3.73*	4,695	*84.53 83.58-85.48*	5,554
Other hysterectomy	35	*8.08 5.51-10.65*	3	*0.69 0-1.47*	395	*91.22 88.55-93.89*	433
Total	**713**	***11.91 11.09-12.73***	**184**	***3.07 2.63-3.51***	**5,090**	***85.02 84.12-85.92***	**5,987**

There were ten deaths in the study population during their hospital admission, five occurred in patients with a cancer diagnosis (5/713, 7 per 1,000) and five in patients with a benign diagnosis (5 from 5,090, 1 per 1,000).

6.3.3.6 Regression analysis of factors associated with operation type

To establish if there were any preoperative patient factors influencing the likelihood of having a total, rather than any other type of hysterectomy, logistic regression analysis was applied. It was predicted that those factors most likely to be associated with operation type were the age of the woman (do older women have less follow-up than younger women?), her deprivation score, the index test result (does an abnormal index test make a certain operation type more likely?).

The result of the index test was categorised into three groups (normal, abnormal or uncertain significance, those never having an index test being excluded). 5,787 women had data on all the variables and were included in the model. Ethnicity was excluded as there were so many missing variables at the outset. Table 69 summarises the analysis run backwards, stepwise fashion.

Thus it may be seen that the presence of an abnormal index test was a significant predictor of whether or not a woman has a total hysterectomy. Age was the other significant factor in the model; with increasing age a woman is more likely to have a total hysterectomy. However deprivation was not associated and was rejected from the model for the final step and is thus not reported in the table.

Table 69. Logistic regression analysis: predictors of type of operation

Variable**	**ß**	**S.E. of ß**	**Sig.**	**Odds ratio**	**95% range for OR**
Age	-0.033	0.005	0.000*	0.968	0.959 - 0.997
Index test: Normal			0.004*		
Index test: Abnormal	-2.178	0.714	0.002*	0.113	0.028 - 0.459
Index test: Unknown	-0.297	0.210	0.157	0.743	0.493 - 1.121
Constant	*-0.924*	*0.226*	*0.000*	*0.397*	

** Significant. **Deprivation is not reported as it was excluded from final step*

The Nagelkerke R Square (R^2) = 0.030 thus this model only explains 3.0% of the likelihood of a woman having a total hysterectomy.

The overall percentage of women who have a total hysterectomy predicted by the model is 92.8%, but this is completely unchanged by the introduction on the variables and as such none of these factors has a significant bearing on the likelihood of any given operation type.

When the model was run again with the addition of the simplified ethnicity data, (white or non-white) for the 3,976 women with all the variables included, it had no impact on the result.

The model was also run using deprivation quintiles instead of deprivation scores, in case this impacted on the results, but it did not have any great impact (Nagelkerke R Square = 0.032, model prediction unchanged at 92.8%) and again deprivation was excluded from the final step.

Thus although the presence of an abnormal index test result and increasing age are associated with subsequent operation type, these are weak predictors.

6.3.4 Summary of section 6.3

This section examined the hysterectomy procedures to establish which variant took place, the diagnosis and at which hospital. This process identified the source of some of the problems with ethnicity coding as hospitals across the region varied widely (14-98%).

The number of operative procedures varied significantly, although, all hospitals identified as having departments of gynaecology, undertook over 150 operations during the year, but individual clinicians varied from 1 to 189 hysterectomies each. There were no clear associations between hospitals with more deprived patients and age at surgery or duration of post operative stay.

There were differences noted between those women having total and sub-total hysterectomies with younger, non-white women being the most likely to undergo the subtotal variant, but no association noted with deprivation score or duration of hospital stay. Having a normal index test result was weakly associated with operation type.

The worst operative diagnosis was established: 11.61% had malignant disease, although this was not necessarily gynaecological. 3.00% had intraepithelial neoplasia or a carcinoma in situ, 2.51% were unclassifiable with the majority having a hysterectomy performed for benign indications.

There were differences detected between the various diagnosis groups with cancer patients being older, more likely to be white and having a longer hospital stay, although the ethnicity data included small numbers. The index cervical screening test result was positively correlated with the final diagnosis but was not a reliable predictor.

6.4 WHAT HAPPENS AFTER HYSTERECTOMY: WHICH WOMEN HAVE VAGINAL VAULT CYTOLOGY TESTS?

6.4.1 Overview of vault smear sub groups

The data were then divided into operation type (total or subtotal hysterectomy), the overall worst diagnosis at time of surgery (benign disease, pre-invasive or malignant / invasive disease) and whether or not women underwent post operative follow-up by means of vaginal vault cytology (vault smear testing). Table 70 gives the numbers and percentages of women in each subgroup and Figure 35 illustrates the breakdown of the various groups in a more visual, flowchart format.

Additionally a further classification as to whether or not women had vault cytology done according to national guidelines was applied – an assessment of 'appropriateness'. This was done as an overview level and then a detailed level to allow for various types of subsequent analysis.

It may be seen that the single largest group is that of women who had a total hysterectomy undertaken for benign indications and who subsequently did not go on to have any vault cytology (N=4,256), representing 69.30% of the study population.

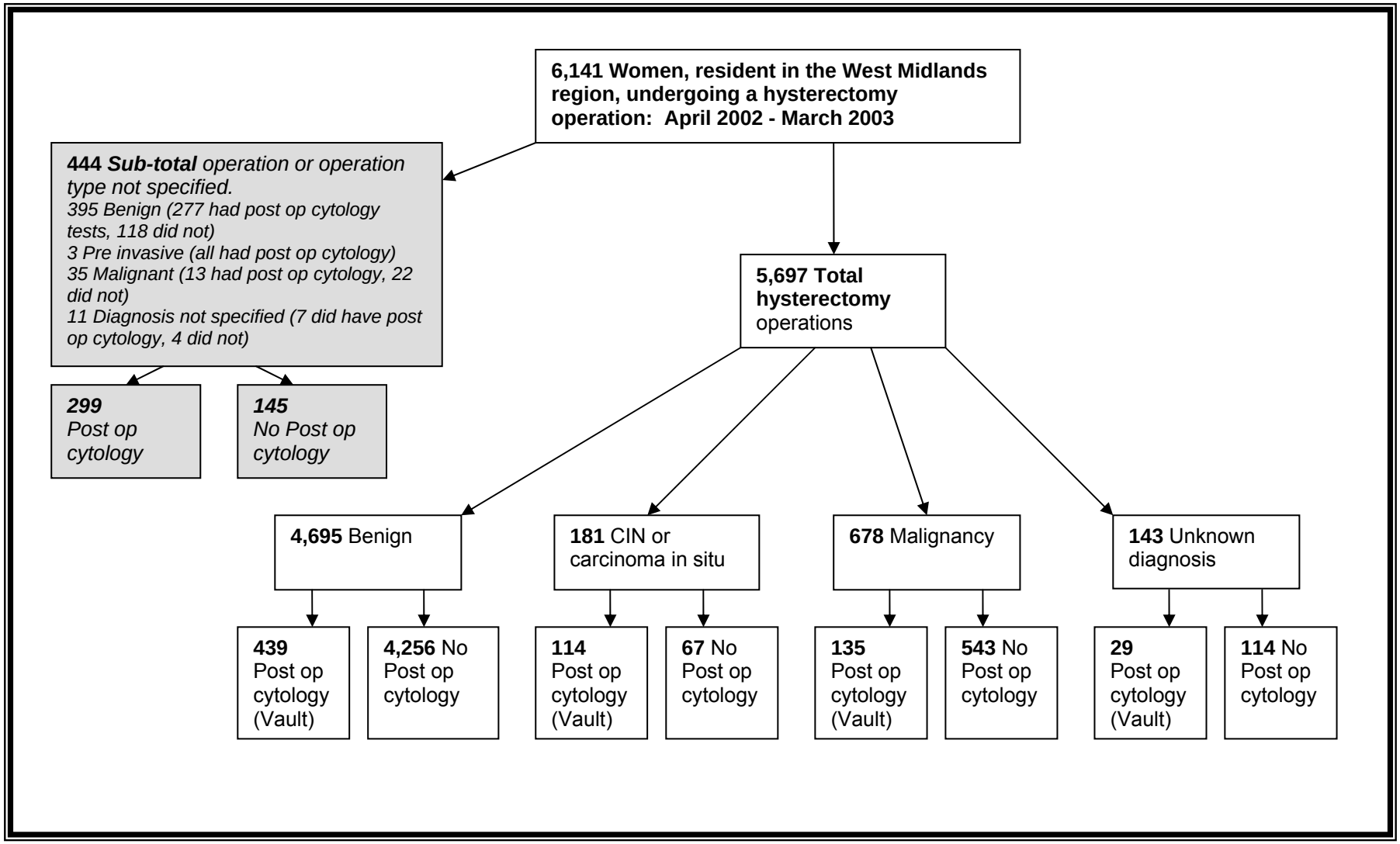
For each of the main groups the proportion of women having vault smears was also calculated and it may be seen that this varied from 9.35% (women having had a total hysterectomy for benign disease) through to 100% in women who had either a sub-total operation or did not have hysterectomy type specified and where the operative diagnosis was carcinoma in situ or cervical intraepithelial neoplasia.

The classification of post operative cytology into appropriate and inappropriate was complex, as screening guidelines have changed over time, the guidelines in place at the time of the hysterectomy (2002-2003) were used to apply a classification of appropriate or inappropriate, this is discussed further in Chapter 7. No national guidelines exist concerning follow-up after malignant disease by means of vaginal vault cytology and so the data for women who had cancers were interesting but the significance was uncertain and they were not explored in depth.

Table 70. Breakdown of numbers of women by hysterectomy type and vault smear testing

Hysterectomy type	Operative diagnosis	N *(%, CI)*	Followed up	N	% Vaults *(CI)*	Subgroups	N	%
Total hysterectomy = 5,697	Malignancy	678 *(11.04, 10.26–11.82)*	No test	543	*19.91 (16.90-22.92)*	-	543	*8.84*
			Post op test	135		-	135	*2.20*
	CIN / Carcinoma in situ (C in-situ)	181 *(2.95, 2.53–3.37)*	No test	67	*62.98 (55.95-70.01)*	-	67	*1.09*
			Post op test	114		Vault cytology tests done exact to protocol (2 with normal results in 24m)	13	*0.21*
						Vault cytology tests done but too many	50	*0.81*
						Vault cytology tests done but too few	24	*0.39*
						Vault cytology tests done but too late	16	*0.26*
						Vault cytology tests done, results abnormal so no guidelines	11	*0.18*
	Benign	4,695 *(76.45, 75.39–77.51)*	No test	4,256	*9.35 (8.52-10.18)*	No post op cytology done correctly	3,958	*64.45*
						No post op cytology but less than 10yrs cytology pre-hysterectomy so too few	298	*4.85*
			Post op test	439		Vault cytology tests done; inappropriate	407	*6.63*
						Vault cytology tests done but <10yrs cervical cytology before op (age less than 35yrs), just one test done so appropriate	16	*0.26*
						Vault cytology tests done but had <10yr cervical cytology before op (age less than 35yr) but >1 so still inappropriate	16	*0.26*
	Unknown	143 *(2.33, 1.95–2.71)*	No test	114	*20.98 (13.69-26.87)*	-	114	*1.86*
			Post op test	29		-	29	*0.47*
Subtotal hysterectomy or type not specified **= 444**	Malignancy	35 *(0.57, 0.38–0.76)*	No test	23	*34.29 (18.86-50.02)*	-	23	*0.37*
			Post op test	12		-	12	*0.20*
	CIN / C in-situ	3 *(0.05, 0–0.11)*	No test	0	*100*	-	0	*0.00*
			Post op test	3		-	3	*0.05*
	Benign	395 *(6.43, 5.82–7.04)*	No test	118	*70.13 (65.62-74.64)*	-	118	*1.92*
			Post op test	277		-	277	*4.51*
	Unknown	11 *(0.18, 0.07–0.29)*	No test	4	*63.64 (35.21-92.07)*	-	4	*0.07*
			Post op test	7		-	7	*0.11*

Figure 35. Flowchart of study participants grouped by operation type and overall diagnosis



6.4.2 Post operative cytology subgroups: description of demographics

The demographic comparisons were made twice, firstly with the whole population of women who underwent post operative cytology and then just in those women who were known to have undergone a total hysterectomy as these women definitely did not have a cervix and thus their cytology was taken from the vaginal vault, these were the population of greatest relevance to the study aims.

6.4.2.1 Whole population post operative cytology

Table 71 summarises the demographic data of the two groups of women: those who had post operative cytology testing and those who did not. Several significant differences were observed with those having post operative cytology being slightly younger (Kruskal Wallis χ^2 = 87.586, 1df, p=<0.001), less deprived (Kruskal Wallis χ^2 = 54.607, 1df, p=<0.001) and more likely to be non-white than the overall population (Pearson χ^2 = 60.402 1df, p= <0.001). There was also an association with shorter post operative hospital stay in this group, however the clinical significance of these observations is uncertain and discussed in Chapter 7.

6.4.2.2 Total hysterectomy group vault cytology

One of the key study aims was to establish the current pattern of follow-up post-hysterectomy by means of vaginal vault cytology.

As only women who have undergone a total hysterectomy can undergo vaginal vault cytology it was important to extract this group from the main data. For the rest of the comparisons and analysis in this chapter, the selected population of just 5,697 women, who we were confident underwent a total hysterectomy, will be used.

When all the analysis of demographic factors was run only on the group of women who had a total hysterectomy, compared with whether or not they under went vault cytology testing, it did not change the overall result of any of the observations outlined in section 6.4.2.1 above (i.e. those having post operative cytology were slightly younger, less deprived, more likely to be non-white and having a shorter post operative hospital stay), although the magnitude of some of the observations varied.

Table 72 summarises all these comparisons; it may be seen that whilst the association with age was slightly weakened, the association with deprivation was strengthened. There was no meaningful change in the results for ethnicity or duration of post operative stay.

Table 71. Summary of differences in demographic data depending on post operative cytology status - whole population

Comparator *Whole study population* *N = 6,141*	**Post operative cytology done** **N = 1,016** % = 16.54	**No post operative cytology testing** **N = 5,125** % = 83.46	**Statistical test**	**Notes**
Age (6,141) *Mean = 51.52* *Median = 48.38* *Skewness = 0.606* *IQR = 18.21*	Mean = 47.57 Median = 45.84 Skewness = 0.796 IQR= 14.41	Mean = 51.76 Median = 49.07 Skewness = 0.527 IQR= 19.86	Kruskal Wallis χ^2 = 87.586 1df, p=<0.001	Thus there was significant association; women who undergo post operative cytology testing tending to be younger than those who do not.
Deprivation (6,141) *Overall Mean = 24.59* *Median = 19.70* *Skewness = 0.847* *IQR = 23.94* <u>Quintiles (N/%)</u> *1 1,628 / 26.51%* *2 1,210 / 19.70%* *3 1,295 / 21.09%* *4 1,177 / 19.17%* *5 831 / 13.53%*	Mean = 28.19 Median = 23.03 Skewness = 0.631 IQR = 29.19 358 / 21.99% 202 / 16.69% 188 / 14.52% 155 / 13.17% 113 / 13.60%	Mean = 23.87 Median = 19.16 Skewness = 0.867 IQR = 23.26 1,270 / 78.01% 1,008 / 83.31% 1,107 / 85.48% 1,022 / 86.83% 718 / 86.40%	Kruskal Wallis χ^2 = 54.607 1df, p=<0.001 Pearson χ^2 = 53.777 4df, p=<0.001 (0 count less than 5)	There was an association established between deprivation score and post operative cytology testing, with those who did undergo post operative testing being somewhat less deprived than those who did not. Analysis of the quintiles confirmed that there was an association detected between deprivation and follow-up by means of cytology testing.
Ethnicity (4,213) *White: 3,842 / 91.19%* *Mixed: 15 / 0.365%* *Asian: 209 / 4.96%* *Black: 119 / 2.82%* *Chinese: 11 / 0.26%* *Other: 17 / 0.40%*	536 / 13.95% 1 / 6.67% 54 / 25.84% 45 / 37.82% 3 / 27.27% 5 / 29.41%	3,306 / 86.05% 14 / 93.33% 155 / 74.16% 74 / 62.19% 8 / 72.73% 12 / 70.59%	Pearson χ^2 = 74.599 5df, p=<0.001 (3 cells count less than 5)	Thus there was an association is demonstrated between ethnicity and use of post operative cytology subsequent to hysterectomy. To remove the effect of small numbers the analysis was re-run using just white/non-white and Pearson χ^2 = 60.402 1df p= <0.001, confirming the finding.
Duration of post op stay (6,136) *Median = 5 days* *Skewness = 6.781* *IQR = 1* *Range = 0 - 81*	Median = 4 Skewness = 12.448 IQR = 2 Range = 0 - 81	Median = 5 Skewness = 5.712 IQR = 2 Range = 0 - 50	Kruskal Wallis χ^2= 13.650 1df, p=<0.001	Thus an association was noted with those who had post operative cytology performed staying in hospital for a slightly shorter time than those who subsequently did not have testing.

Table 72. Summary of differences in demographic data and vault cytology status - total hysterectomy only

Comparator *Total hysterectomy only* *N = 5,697*	**Vault cytology done** **N = 716** % = 12.57	**No vault cytology testing** **N = 4,976** % = 87.34	**Statistical test**	**Notes** *Only including those who underwent a total hysterectomy operation*
Age (5,697) *Mean = 51.44* *Median = 48.88* *Skewness = 0.562* *IQR = 18.78*	Mean = 48.50 Median = 46.93 Skewness = 0.632 IQR = 16.49	Mean = 51.87 Median = 49.17 Skewness = 0.541 IQR = 19.22	Kruskal Wallis χ^2 = 34.446 1df, p=<0.001	Thus there was a significant association with women who undergo vault cytology testing tending to be younger than those who do not.
Deprivation (5,697) *Overall Mean = 24.48* *Median = 19.65* *Skewness = 0.849* *IQR = 23.61* <u>Quintiles (N/%)</u> *1 1,490 / 26.15%* *2 1,139 / 19.99%* *3 1,205 / 21.15%* *4 1,086 / 19.06%* *5 777 / 13.64%*	Mean = 29.46 Median = 26.26 Skewness = 0.510 IQR = 28.84 268 / 17.99% 149 / 13.08% 130 / 10.79% 94 / 8.66% 76 / 9.78%	Mean = 23.77 Median = 18.94 Skewness = 0.896 IQR = 22.87 1,222 / 82.01% 990 / 86.92% 1,075 / 89.21% 992 / 91.34% 701 / 90.22%	Kruskal Wallis χ^2 = 63.173 1df, p=<0.001 Pearson χ^2 = 64.100 4df, p=<0.001 (0 count less than 5)	There was an association established between deprivation score and vault cytology testing, with those who did undergo post operative testing being somewhat less deprived than those who did not. Analysis of the quintiles confirms that there was an association between deprivation score and follow-up by means of vault cytology testing.
Ethnicity (3,918) *White: 3,583 / 91.45%* *Mixed: 13 / 0.33%* *Asian: 196 / 5.00%* *Black: 102 / 2.60%* *Chinese: 8 / 0.20%* *Other: 16 / 0.41%*	372 / 10.38% 1 / 7.69% 46 / 23.47% 30 / 29.41% 2 / 25.0% 5 / 31.25%	3,211 / 89.62% 12 / 92.31% 150 / 76.53% 72 / 70.59% 6 / 75.0% 11 / 68.75%	Pearson χ^2 = 71.074 5df, p=<0.001 (3 cells count less than 5)	There was an association demonstrated between ethnicity and use of vault cytology subsequent to hysterectomy. To remove the effect of small numbers the analysis was re-run using just white/non-white and Pearson χ^2 = 64.305 1 df p= <0.001, confirming the result.
Duration of post op stay (5,692) *Median = 5 days* *Skewness = 6.969* *IQR = 1* *Range = 0 - 81*	Median = 4 Skewness = 9.339 IQR = 3 Range = 0 - 81	Median = 5 Skewness = 5.549 IQR = 1 Range = 0 - 50	Kruskal Wallis χ^2 = 14.405 1df, p=<0.001	Thus an association was noted with those who subsequently had vault cytology done staying in hospital for a slightly shorter time than those who subsequently did not have testing.

6.4.3 Vault cytology status and cervical screening history

Considering only those women who underwent a total hysterectomy, two sets of further comparisons were undertaken against the status of whether or not women underwent vaginal vault cytology testing subsequent to hysterectomy. These were result of the index test and the classification of the entire cervical screening history.

6.4.3.1 Index test compared with vault cytology status

Initially, a cross tabulation of result of the index test, comparing whether or not women had any vault cytology subsequent to hysterectomy, was undertaken (Table 73). This gave a highly significant association; Pearson χ^2 = 382.828, 3df, p=<0.001 (with no cells counting less than 5). Those women whose index result was of uncertain significance and those women who did not have any preoperative testing were subsequently excluded and the comparison rechecked and again, Pearson χ^2 = 345.399 1df p=<0.001 (0 cells count less than 5), thus there was an association between having an abnormal index test result and subsequently having vaginal vault cytology performed.

Table 73. Index test result compared with having vault smear tests

Index test result	Vault test	No vault	Total
Index Abnormal	103	74	177
Index Normal	520	4,236	4,756
Index Uncertain	81	355	436
No pre-op testing	13	315	328
Totals	***717***	***4,980***	***5,697***

6.4.3.2 Entire screening history compared with vault cytology status

The proportion of women in each of the 13 screening history bands was divided into whether or not they underwent vault cytology testing. Table 74 summarises these data. Cross tabulation gave a significant Pearson χ^2 = 406.540 (12df p=<0.001, but 4 cells counted less than 5).

Table 74. Entire screening history compared with vault cytology status

Group	Vault test	No vault	% Vault observed (*CI*)	Total
Index abnormal, previous abnormal	83	100	45.36 (*38.15 – 52.57*)	183
Index abnormal, previous only normal	57	125	31.32 (*24.38 – 38.06*)	182
Index abnormal, previous uncertain	68	120	36.17 (*29.30 – 43.04*)	188
Index abnormal, no prior tests	10	15	40.00 (*20.80 – 59.20*)	25
Index normal, previous abnormal	122	829	12.83 (*10.70 – 14.96*)	951
Index normal, previous only normal	233	2,359	8.99 (*7.89 – 10.09*)	2,592
Index normal, previous uncertain	93	806	10.34 (*8.35 – 12.33*)	899
Index normal, no prior tests	19	178	9.64 (*5.52 – 13.76*)	197
Index uncertain, previous abnormal	6	26	18.75 (*5.23 – 13.76*)	32
Index uncertain, previous only normal	5	45	10.00 (*1.68 – 18.32*)	50
Index uncertain, previous uncertain	3	35	7.89 (*0 – 16.46*)	38
Index uncertain, no prior tests	1	6	14.29 (*0 – 40.22*)	7
Never had preoperative testing	17	336	4.82 (*2.59 – 7.05*)	353
Totals	***717***	***4,980***	**-**	***5,697***

The ‘index uncertain’ and never preoperative tested groups were then excluded because of small numbers, for the remaining eight groups a Pearson χ^2 = 369.972 (7df p=<0.001, 1 cell count less than 5), thus still a highly significant finding so there were associations between different patterns of cervical screening and having vault cytology testing subsequent to total hysterectomy.

Then, some of the sub-groups were compared directly and demonstrated clear differences between the groups: women who only ever had normal screening (n=2,592) were compared with those who repeatedly had abnormal screening (n=183) preoperatively, Pearson χ^2 = 224.024 (1df p=<0.001).

When repeated with the rest of the population compared as a third group (n=2,922) with those two groups again a significant difference was obtained with Pearson χ^2 = 213.444 (2df p=<0.001). Thus, as the simple percentages in Table 74 would suggest, the likelihood of having vault cytology post operatively is associated with the results of preoperative screening history.

6.4.4 Vault cytology status and operative diagnosis

For those women who underwent a total hysterectomy, a cross tabulation of the final operative diagnosis (4 groups, Table 75) compared with whether or not women had any vault cytology subsequent to hysterectomy was undertaken) and this gave a highly significant result of Pearson χ^2 = 503.311, 3df, p=<0.001 (0 cells count less than 5). Those women whose operation result was of uncertain significance were subsequently excluded and the Pearson χ^2 = 502.203, 2df p=<0.001 (0 cells count less than 5), thus confirming there was clearly a strong association between operative diagnosis and subsequently having vaginal vault cytology.

Table 75. Summary of diagnosis at time of surgery and use of vault cytology

Diagnosis	Vault test	No vault	% Vault (*CI*)	Total
Cancer	135	543	19.91 (*16.90 – 22.92)*	678
CIN	114	67	62.98 (*55.95 – 70.71*)	181
Benign	439	4,256	9.35 (*8.52 – 10.18*)	4,695
Uncertain	29	114	20.28 (*13.69 – 26.87*)	143
Totals	***717***	***4,980***	***12.59*** (*11.73 – 13.45*)	***5,697***

6.4.5 Factors associated with a woman having vault cytology post operatively

One of the principal aims of the study was to establish which factors may be associated with a woman having cytology testing post operatively compared with not having any testing. Having already investigated various possible factors independently (Table 72), logistic regression analysis was undertaken.

6.4.5.1 Patient factors associated with having vault cytology

It was postulated that those factors most likely to be associated with having vault cytology were the operation type (i.e. total hysterectomy where the cervix is removed or subtotal), the deprivation status of the patient, her age at hysterectomy, her diagnosis and what the result of her last cervical smear test was (the index result). The operative diagnosis was categorised into four groups (benign, pre-malignant, malignant and unknown) and the result of the index test into three groups (normal, CIN, invasive).

The analysis is reported in Table 76, run in backwards stepwise fashion, but when repeated with forward stepwise analysis the result was the same. Women who never had any cytology were excluded from the analysis as were women who did not have a total hysterectomy and so there were 5,237 women included in the model. As 87.1% of women never had any vault cytology this was the overall starting point.

Table 76. Predictors of having vault cytology tests in women undergoing total hysterectomy*

Variable	ß	S.E. of ß	Sig.	Odds ratio	95% range for OR
Age	-0.018	0.004	<0.000	0.982	0.974 - 0.989
Deprivation score	0.019	0.002	<0.000	1.019	1.014 - 1.025
Diagnosis: Benign	-	-	<0.000	-	-
Diagnosis: Uncertain	1.072	0.127	<0.000	2.921	2.278 - 3.745
Diagnosis: Cancer	0.924	0.125	<0.000	7.023	1.972 - 14.927
Diagnosis: Pre-malignant	2.326	0.192	<0.000	10.239	6.546 - 13.768
Index test: Normal	-	-	<0.000	-	-
Index test: Invasive	1.058	0.205	<0.000	2.882	1.928 - 4.308
Index test: Dyskaryosis	0.319	0.136	0.034	1.357	1.023 -1.801
Constant	*-1.890*	*0.215*	*<0.000*	*0.151*	-

** Backward, stepwise, logistic regression analysis*

It may be seen that all the suggested variables were significant predictors of whether or not a woman has post operative vault cytology. Age was negatively associated, suggesting that younger women were more likely to have vault cytology than older women, however with an odds ratio of 0.98 this was of limited clinical usefulness.

Deprivation had an odds ratio of 1.019, thus for each point increase in IMD07 score there was a slightly increased likelihood of having vault cytology. However, IMD07 is not a linear scale and our study participants had scores of up to 80 and so the usefulness of this association may be questioned. The odds ratios of an invasive test result at index cervical smear of 2.882 and of dyskaryosis of 1.357 were significantly more meaningful in practice.

However, Nagelkerke R^2 = 0.157 thus this model only explains 15.7% of the likelihood of a woman having post operative cytology. Using a 50% cut off, the overall percentage of positive and negative (vault/no-vault) correctly predicted by the final fitted model was 88.20%.

The analysis was then repeated including those women who were known to have a subtotal operation, as well as a total hysterectomy or in whom operation type could not be established. There was sufficient data on 5,787 women and the results are reported in Table 77.

Operation type was the most significant predictor of having post operative testing (Odds ratio of 17.986) and including it in the model increased the accuracy of the model (Nagelkerke R^2 =0.282) thus this model now explains 28.2% of the likelihood of a woman having post operative cytology.

Table 77. Regression analysis: predictors of having post operative cytology tests for any woman undergoing a hysterectomy

Variable	ß	S.E. of ß	Sig.	Odds ratio	95% range for OR
Operation type	2.890	0.118	<0.000	17.986	14.268 - 22.674
Age	-0.021	0.004	<0.000	0.979	0.972 - 0.986
Deprivation Score	0.016	0.002	<0.000	1.017	1.012 - 1.021
Diagnosis: Benign	-	-	<0.000	-	-
Diagnosis: Uncertain	0.757	0.217	<0.000	2.131	1.394 - 3.258
Diagnosis: Cancer	0.924	0.125	<0.000	2.520	1.972 - 3.220
Diagnosis: Pre-malignant	2.251	0.190	<0.000	9.493	6.546 - 13.768
Index test: Normal	-	-	<0.000	-	-
Index test: Invasive	1.106	0.194	<0.000	3.023	2.065 - 4.424
Index test: Dyskaryosis	0.319	0.136	0.019	1.376	1.054 -1.796
Constant	*-4.509*	*0.246*	*<0.000*	*0.011*	-

However, the overall percentage predicted by the model is actually worse at 86.9%. Thus the original model applied only to women know to have had a total hysterectomy, is preferred.

Regression analysis was then repeated using deprivation quintiles instead of deprivation score and also using age, banded into five-year groups. Both models gave results very similar to the first model with slightly less accuracy and are not reported further.

6.4.5.2 Site of treatment associated with having vault cytology

As patient factors had been explored extensively and were found to have only limited power to predict likelihood of having vault cytology post operatively, hospital factors were introduced into the analysis.

The hospital for each total hysterectomy operation was included in the model, with the 17 main centres. that had been coded accurately. included. Women were excluded if they had never had any cytology. The reference category was taken to be a large tertiary referral centre. This left 4,515 women available for inclusion in the analysis.

Table 78 summarises the raw data concerning hospitals and vault cytology. When regression analysis was re-run including hospital of treatment, it was noted to be significant in the model (Nagelkerke R^2 = 0.198) although making little difference to the ability of the model to predict who does and does not have vault cytology.

Cross tabulation was undertaken to investigate this association and gave Pearson χ^2 = 159.244 (15df, p<0.001). Thus women appear to be more or less likely to have vault cytology depending on which hospital the hysterectomy is conducted at. A range of 4.9% to 25.7% of cases having subsequent vault cytology was noted. The reference institution had the highest rates; this was a tertiary referral centre for gynaecological oncology cases.

Table 78. Vault cytology testing, by hospital of surgery, in women having a total hysterectomy

Code for hospital of hysterectomy surgery	Vault cytology	% (*CI*)	No vault cytology	%	Total
1 (Reference institution)	142	25.72 (*22.07 – 29.37*)	410	74.28	552
2	34	15.25 (*10.53 – 19.97*)	189	84.75	223
3	7	5.11 (*1.42 – 8.80*)	130	94.89	137
4	19	9.79 (*5.60 – 13.97)*	175	90.21	194
5	72	20.63 (*16.38 – 24.88*)	277	79.37	349
6	30	9.23 (*6.08 – 12.38*)	295	90.77	325
7	17	12.14 (*6.73 – 17.55*)	123	87.86	140
8	54	15.04 (*11.34 – 18.74*)	305	84.96	359
9	25	7.69 (*4.79 – 10.59*)	300	92.31	325
10	45	12.61 (*9.17 – 16.05*)	312	87.39	357
11	37	21.76 (*20.20 – 35.44*)	133	78.24	170
12	52	21.58 (*16.39 – 26.77)*	189	78.42	241
13	55	17.19 (*13.06 – 21.32*)	265	82.81	320
14	7	4.90 (*1.36 – 8.44*)	136	95.10	143
15	19	5.99 (*3.38 – 8.60*)	298	94.01	317
16	35	9.28 (*6.35 – 12.21*)	342	90.72	377
Total (used in model)	**650**	**14.35** (*13.33 – 15.37)*	**3,879**	**85.66**	**4,529**
Hospital outside region or no gynaecology on-site or invalid code	*67*	*7.83* (*6.03 – 9.63*)	*789*	*92.17*	*856*
Total	***717***	***13.31*** (*12.40 – 14.22*)	***4,668***	***86.68***	***5,385***

6.4.6 Adherence to national screening guidelines: factors associated with appropriate use of vault cytology testing

To establish if there were any factors influencing the likelihood of a woman having appropriate vaginal vault cytology, in addition to her diagnosis at surgery, logistic regression analysis was undertaken separately for the two groups of women where national guidelines clearly apply. Thus, women having a total hysterectomy where the operative diagnosis is either benign disease (no vault smears) or CIN (2 vault smear tests in 2 years). For the purposes of regression analysis no further classification was possible as the group of women having malignant disease was too small to allow for meaningful results.

6.4.6.1 Appropriate use of vault smears: women with a diagnosis of CIN at total hysterectomy

Intraepithelial neoplasia was detected in 181 women at the time of total hysterectomy, of these 114 subsequently had post operative vault cytology (63.0%) which is in line with national screening guidelines, however 67 did not.

Logistic regression analysis was undertaken on this subgroup of women who should all be having post operative vault cytology. It was postulated that those factors most likely to be associated with these women having a vault test in accordance to guidelines were the age of the patient, deprivation status and the result of the index test (normal, abnormal or uncertain significance).

Table 79 summarises the analysis run backwards, stepwise fashion, excluding ethnicity as there were so many missing variables.

Table 79. Logistic regression analysis: predictors of adherence to national guidelines for women having CIN

Variable	ß	S.E. of ß	Sig.	Odds ratio	95% range for OR
Age	*-0.15*	*0.014*	*0.279*	*0.985*	*0.960 - 1.1012 **
Deprivation Score	0.017	0.010	0.096	1.018	0.997 - 1.039
Index test: Normal	-	-	0.009*	-	-
Index test: Abnormal	1.101	0.361	0.001*	3.143	1.559 - 6.338
Index test: Unknown	0.507	0.493	0.304	1.661	0.631 - 4.368
Constant	*-0.434*	*0.359*	*0.227*	*0.648*	

** Significant*

Thus, it may be seen that only the presence of an abnormal index test was a significant predictor of whether or not a woman had any post operative vault cytology undertaken appropriately. With an odds ratio of 3.143 for an abnormal result and 1.661 for a result of uncertain significance, Nagelkerke R^2 = 0.110 thus, although helpful, this model only explains 11.0% of the likelihood of a woman having post operative cytology appropriately.

The overall percentage of women adhering / not adhering to guidelines, predicted by the final model (using 50% cut off), was 67.6% compared with the 64.8% of women who were already in the 'appropriate' group on the basis of operative diagnosis alone.

6.4.6.2 Appropriate use of vault smears: women with a diagnosis of benign disease at total hysterectomy

4,695 women had a diagnosis of benign disease at the time of total hysterectomy, of these 4,256 did not have any post operative vault cytology (90.6%) which is in line with national screening guidelines[84], however, 439 had subsequent vault cytology, outside of the guidelines.

Binomial logistic regression analysis was undertaken of this subgroup of women who should not be having any vault cytology: it was predicted that those factors most likely to be associated were the age of the patient, her deprivation status and ethnic group and the result of her last cervical smear test (index). The result of the index test was categorised into three groups (normal, abnormal, uncertain significance).

Table 80 summarises the analysis run backwards, stepwise fashion and excludes the ethnicity data (too many missing variables). The analysis was also run using deprivation quintile but this did not impact on the outcome and is not reported further.

Decreasing age, increasing deprivation score and worsening result of index cytology were all predictors of adherence to national guidelines, however only the presence of an abnormal index test had an odds ratio of more than 1.5 (Table 80).

Table 80. Logistic regression analysis: predictors of adherence to national guidelines for women having a benign diagnosis

Variable	ß	S.E. of ß	Sig.	Odds ratio	95% range for OR
Age	-0.018	0.005	<0.000*	0.982	0.973 - 0.991
Deprivation score	0.022	0.003	<0.000*	1.023	1.017 - 1.028
Index test: Normal			<0.000*		
Index test: Abnormal	1.313	0.335	<0.000*	3.718	1.926 - 7.174
Index test: Unknown	0.300	0.182	0.099	1.350	0.945 - 1.930
Constant	*-1.999*	*0.253*	*0.0008*	*0.135*	

** Significant*

Although all the suggested variables were significant predictors of whether or not a woman has a post operative vault cytology, with Nagelkerke R^2 =0.048 this model only explains 4.8% of the likelihood of a woman having post operative cytology, a very small proportion. Using a 50% cut off, the overall percentage of adherence/non adherence to guidelines predicted by the final model is 90.3% and this was unchanged from the original (226 cases were excluded because of missing data). Thus, none of the factors significantly influences the likelihood of a woman having inappropriate vault cytology beyond the impact of her original operative diagnosis.

The analysis was also run including the ethnicity data dichotomised into white and non-white (in view of the small numbers), but the outcome was the same with no difference in the prediction after all factors were accounted for (3,084 cases included), although the Nagelkerke R^2 =0.078 thus explaining 7.8% of the likelihood of a woman having post operative cytology, but the overall percentage predicted by the final model was unchanged.

6.4.7 Factors associated with having an abnormal vault cytology result

The final stage in the analysis was to examine the vaginal vault cytology test results more closely to determine which were 'normal' or 'abnormal' test results and to establish if there were any factors associated with an increased likelihood of having an abnormal result.

Women who had a total hysterectomy (n=5,687) and who ever had a vault cytology test (n=717) were divided into those who only ever had normal cytology, those who had one or more abnormal results and those who had one or more uncertain results (where the remainder were normal). They were then subdivided into groups based on numbers of vault tests that they ever had (one, two or more than two), and what that woman's result at hysterectomy had been: see Table 81.

It may be seen (Table 81) that of the 717 women who underwent vault cytology, the great majority (79.50%, CI *76.55 – 82.45%)* only ever had entirely normal results. However, 17.57% (*14.78 – 20.36%)* had at least one result which was of uncertain significance, but only a very small proportion, 2.93% (*1.70 – 4.16%)*, ever had any abnormal vault smear results.

When just those women who had greater than two vault tests in total were examined, women having abnormal or results of uncertain significance, appeared to have a greater total number of tests (range 3 - 10, 7 groups) than those women with normal results, Fishers Exact test (Monte Carlo method) = 34.399, 14df, p=<0.001.

Table 81. Vault cytology results (total hysterectomy only)

Results per woman	Number of vault tests	Diagnosis at hysterectomy				Total number
		Malignancy	CIN/in-situ	Benign	Unknown	
Normal results only N = 570	1	48	20	283	6	357
	2	19	19	70	4	112
	>2, *range 3 - 7 median = 3.00*	33	38	23	7	101
Abnormal (1 or more) N = 21	1	1	2	1	0	4
	2	0	0	3	0	3
	>2, *range 3 - 7 median = 5.50*	1	8	2	3	14
Uncertain (1 or more) N = 126	1	5	1	11	0	17
	2	8	2	21	1	32
	>2, *range 3 - 10 median = 5.00*	20	24	25	8	77
Subtotal	*-*	*135*	*114*	*439*	*29*	*717*
	Not tested	543	67	4,256	114	4,980
Totals	***-***	***678***	***181***	***4,695***	***143***	***5,697***

Diagnosis at time hysterectomy is the basis for national screening guidelines concerning use of vaginal vault cytology in women who had CIN. Cross tabulation of the final operative diagnosis (Cancer, CIN, benign) and the vault cytology result (normal, abnormal, uncertain) confirmed that a strong association existed: Pearson χ^2 = 35.874, 4 df p=<0.001 (2 cells count less than 5).

Comparisons were then made between those women having normal and abnormal vault test results in terms of age, deprivation, ethnicity and duration of post operative hospital stay, in an effort to establish any demographic patient factors that may predict likelihood of a woman having abnormal vault cytology result.

These findings are summarised in Table 82 which also includes, for ease of comparison (but not for analysis in view of small numbers), those women who had uncertain results and those who did not have vault cytology (shaded out).

It may be seen that there were no meaningful, demographic, differences between those women having normal and abnormal vault cytology detected and thus multiple regression analysis was not undertaken.

Table 82. Summary of differences in demographic data between those having differing vault test results

Comparator *All women having total hysterectomy* *N = 5,697*	**No vault Cytology** **N = 4,980** **% = 87.41**	**Vault cytology 'normal'** **N = 570** % = 10.01	**Vault cytology 'abnormal'** **N = 21** % = 0.37	**Vault cytology 'uncertain'** **N = 126** % = 2.21	**Statistical test** *(2 group comparisons)*	**Notes** *(comparing just abnormal vs normal vault test results; 2 group results)*
Age (5,697) *Mean = 51.44* *Median = 48.88* *Skewness = 0.562* *IQR = 18.78*	Mean = 51.87 Median = 49.17 Skewness = 0.541 IQR = 19.20	Mean = 48.61 Median = 47.67 Skewness = 0.622 IQR = 15.84	Mean = 51.43 Median = 47.07 Skewness = 0.768 IQR = 21.55	Mean = 47.536 Median = 44.244 Skewness = 0.564 IQR = 18.12	Kruskal Wallis χ^2= 0.278 1df, p=0.598	Although an association exists between age and having vault tests, when the analysis was done comparing just normal and abnormal groups the association disappeared.
Deprivation (5,697) *Overall Mean = 24.48* *Median = 19.65* *Skewness = 0.849* *IQR = 23.61* Quintiles (N/%) *1 1,490 / 26.15%* *2 1,139 / 19.99%* *3 1,205 / 21.15%* *4 1,086 / 19.06%* *5 777 / 13.64%*	Mean = 23.76 Median = 18.91 Skewness = 0.897 IQR = 22.87 1,222 / 82.01% 990 / 86.92% 1,075 / 89.21% 992 / 91.34% 701 / 90.22%	Mean = 29.299 Median = 25.640 Skewness = 0.491 IQR = 29.16 212 / 14.23% 115 / 10.10% 105 / 8.71% 76 / 7.00% 62 / 8.00%	Mean = 27.806 Median = 25.400 Skewness = 1.164 IQR = 20.63 6 / 0.40% 6 / 0.53% 6 / 0.50% 1 / 0.09% 2 / 0.26%	Mean = 30.295 Median = 26.960 Skewness = 0.529 IQR = 30.00 50 / 3.36% 28 / 2.46% 19 / 1.58% 17 / 1.56% 12 / 1.54%	Kruskal Wallis χ^2= 0.203 1df, p=0.653 Fishers exact = 1.176, 4df, p=0.900 (2sided)	There was no association established between deprivation score and having abnormal vault cytology. The analysis of quintiles rather than crude IMD07 score confirms that no association was detected.
Ethnicity (3,918) *White: 3,583 /91.45%* *Mixed: 13 / 0.33%* *Asian: 196 / 5.00%* *Black: 102 / 2.60%* *Chinese: 8 / 0.20%* *Other: 16 / 0.41%*	3,211 / 89.62% 12 / 92.31% 150 / 76.53% 72 / 70.59% 6 / 75.0% 11 / 68.75%	303 / 8.46% 1 / 7.69% 41 / 20.92% 26 / 25.49% 1 / 12.50% 2 / 12.50%	12 / 3.35% 0 / 0% 1 / 0.51% 0 / 0% 1 / 12.50% 0 / 0%	57 / 1.59% 0 / 0% 4 / 2.04% 4 / 3.92% 0 / 0% 3 / 18.75%	Fishers exact (for 2x2) Sig 0.755 - 0.345.	Many cells had numbers <5 so analyses run on the white / non-white groups only; no association was detected.
Duration of post op stay (5,692) *Median = 5 days* *Skewness = 6.969* *IQR = 1* *Range = 0 - 81*	Median = 5 Skewness = 5.549 IQR = 1 Range = 0 - 50	Median = 4 Skewness= 3.883 IQR = 2 Range = 0 - 38	Median = 5 Skewness = 0.272 IQR = 2 Range = 0 - 10	Median = 5 Skewness = 9.468 IQR = 3 Range = 0 - 81	Kruskal Wallis χ^2= 0.004 1df, p=0.951	There were no differences detected between those having normal and abnormal vault cytology.

6.4.8 Summary of section 6.4

This final section of results considered the four years following surgery, when some women were followed up by post operative cytology. Those with a subtotal hysterectomy should have remained in the national cervical screening programme and thus were excluded from the analysis. Women having a total hysterectomy should only have had vaginal vault cytology testing if they had CIN or, in the case of malignancy, if their consultant had requested it.

Vault cytology was undertaken inappropriately on 9.35% (CI 8.52 – 10.18) of those women having total hysterectomy for benign indications, and was inappropriately not undertaken on 37.02% of women with CIN. Of those with CIN who were followed up, this was frequently not according to protocol specified intervals and only 13 women with CIN (of 181) had screening completely compatible with the recommended intervals, 11 had an abnormality on their first test so the guidelines ceased to apply.

Operative diagnosis was the strongest predictor of having any subsequent vault cytology, which tended to occur in younger, less deprived non-white women who had an abnormal index test result. Although age and deprivation were significantly associated with having vault cytology the odds ratios were very small and the clinical usefulness of this finding is limited.

Hospital site of surgery was found to be associated with having vault cytology but did not influence the overall predictive power of the regression model. The reference institution (a tertiary referral centre) was the most likely to have patients who subsequently had vault cytology.

Widespread inappropriate use of vault cytology testing was evident, however regression analysis failed to establish many associated factors, with presence of an abnormal index test as the only genuine predictor.

Abnormal vault cytology test results were very uncommon with only 21 true abnormalities detected and only 2.93% (CI 1.70 - 4.16%) of those women who have vault cytology every having an abnormal result.

6.5 SUMMARY OF RESULTS CHAPTER

This chapter has systematically considered the study data in four main sections with multiple comparisons. Several graphs, figures and tables have been used in an attempt to present the data in a meaningful way and the explanation of the analysis has focussed on clinical importance of the findings.

Study population demographics

The overall study population demographics revealed an incidence of hysterectomy of 23 per 10,000, and a median age of surgery of 48 years. Age standardisation had little bearing on these findings. Age specific incidence rates varied, with the highest rate in women aged 44 – 49yrs (63 per 10,000 pa).

Deprivation scores were very similar to the West Midlands region, which is somewhat more deprived than England overall. Variability in hysterectomy incidence, by deprivation quintile, revealed a clear correlation between women living in more deprived areas being more likely to have a hysterectomy operation (incidence of 25 per 10,000 vs 20 per 10,000 for most and least deprived quintiles).

Ethnicity, although only available for two thirds of the population, indicated that the study population had some differences from background population of the West Midlands region: Caribbean and White women were over represented and Indian women were under represented.

Using age standardised data a significant difference was noted between the three main ethnic groups (White, Black and Asian).

Ten women died during their hospital admission, five of whom had malignant disease. This represented 0.16% of the study population or a mortality rate of 16 per 100,000 hysterectomy operations.

Cervical screening history

Preoperative cervical screening was undertaken on 5,787 women (94.23%). Those ever tested underwent a median of five tests each, although this varied significantly by age. Post operative cytology was performed on one in six of the whole cohort. The result of last cervical screening test before hysterectomy (the index test), suggested that severe changes were more common in younger women and abnormal test results were more likely in women living in more deprived regions. Ethnicity was not associated with index test result. Overall women in the study tended to have more cytological screening than the general population when they were younger.

Use of a complex algorithm from the WMQARC allowed entire screening histories to be classified and compared; findings corroborated the data on deprivation and ethnicity even though the groupings were undertaken slightly differently from that of the raw study data.

Outcome of hysterectomy

Consideration of the different hospitals revealed some of the causes of poor ethnicity data with some hospitals clearly using invalid coding whereas others had up to 98% of patients ethnicity recorded. Operation type was established for all but eight of the participants. Sub-total surgery was more common in younger women and total hysterectomy was more common in white women. 11.61% of the study population had a hysterectomy for a malignancy (not necessarily gynaecological), 3% for intraepithelial neoplasia of all types but the great majority had benign indications.

Women with malignant disease were significantly older than the rest and white women were more likely to have a diagnosis of malignancy. Regression analysis of those factors associated with having a total or subtotal type of hysterectomy revealed significant associations with age and result of the index test, however these only accounted for a small proportion of the total.

Vault cytology

Dividing the study participants according to hysterectomy type allowed post-operative cytology to be classified as vault cytology or cervical screening. The group of women who had total hysterectomies were then considered further.

Vault cytology was undertaken on 9.35% of women, who had hysterectomies for benign disease, this was clearly inappropriate.

Of women having hysterectomy for carcinoma in situ or CIN only 63% had any vault cytology, thus in the group of women who are explicitly recommended to have some post operative testing, over a third do not have any.

The women having CIN were examined more closely; in addition to those not being tested at all, of those who were tested, 24 only had one test, 16 had two tests but over too great a time frame (>2yrs), 50 had more than two consecutive normal results (so excessive testing) and just 13 (7.18%) were followed up exactly in accordance with the national guidelines.[16]

When those women having benign disease were considered more closely, (Table 70), and latest guidance applied, (including the suggestion that vault cytology be undertaken if a woman has less than 10 years of pre-hysterectomy cervical screening) the proportion having inappropriate testing became even worse, with inappropriate screening in 721 of 4,695 = 15.36%.

Operative diagnosis was, appropriately, confirmed as the strongest predictor of having vault cytology. Women who had vault cytology undertaken were more likely to be younger, less deprived and non-white than those who did not have vault testing. Having an abnormal index test result was clearly associated with having post operative cytology as was having a history of any abnormal cytology preoperatively.

Logistic regression analysis demonstrated that age and deprivation score were also associated with having vault cytology but the odds ratios were very small and the clinical usefulness of this observation is in doubt. Hospital of surgery was also a significant factor but overall impacted little on the fitted model.

Regression analysis of those factors associated with inappropriate usage of vault cytology only identified index test result as being clinically important although age and deprivation score were related. The only factor associated with having an abnormal vault test result was diagnosis at time of surgery, however with only 21 definitely abnormal vault test results from 717 (2.93%) it was not possible to draw firm conclusions. Regression analysis could not be undertaken in view of the small numbers.

Overview of results

Thus analysis of the study dataset confirms that hysterectomy is still commonly performed for benign indications in the West Midlands, ethnicity and deprivation are related to incidence of surgery. Ten women died during their hospital admission, a mortality rate of 16 per 10,000 hysterectomy operations or one per 625 cases, five of these had malignant disease. Preoperative screening history is associated with likelihood of having post operative vault cytology testing and women had a median of five cervical screening tests prior to hysterectomy.

Vault cytology testing is being undertaken inappropriately in a significant proportion of cases although the only factor of clinical importance associated was the presence of abnormal index cytology. Less than 3%, of those tested, had abnormal results at vault cytology testing.

CHAPTER SEVEN: DISCUSSION

INTRODUCTION TO CHAPTER

This chapter draws together all phases of the study, by first summarising the background to the research including key findings from the literature review and results of preliminary work undertaken by the author. It then examines the study methodology and the limitations and challenges of this particular project. The important study findings are considered next, presented in the same order as the results (Chapter 6), contextualising them and suggesting possible explanations. Finally, this chapter considers the implications of these findings in practice and makes recommendations for the future.

7.1 BACKGROUND TO THE RESEARCH

Hysterectomy is one of the most common major surgical operations undertaken on women, with approximately 20% of UK women undergoing this procedure during their lifetime.[2] Any operation carries a degree of risk, even when undertaken in optimal conditions, consequently 8.5% of women experience a minor adverse event from hysterectomy and 4.4% a major one.[57]

There are several variants of hysterectomy operations;[32] key to this study is the differentiation between a total hysterectomy, which involves removal of the uterine cervix and sub-total hysterectomy which leaves the uterine cervix in situ.

Other variants of hysterectomy include the choice of surgical route i.e. abdominal, vaginal or laparoscopically assisted, and how much additional tissue is removed i.e. bilateral salpingooophrectomy involves removal of the Fallopian tubes and ovaries; radical hysterectomy includes removal of substantial portions of lymphatic tissue and other structures including para-cervical tissue.

Cervical screening is well established in the UK with the aim of preventing cervical cancer, the NHS Cervical Screening Programme (NHSCSP) is one of the most successful programmes worldwide and is credited with a 42% reduction in the incidence of cervical cancer within a decade of its establishment.[15]

Total hysterectomy is a reason for ceasing routine recall from the NSHCSP as the cervix is no longer present. Follow-up after total hysterectomy by means of vaginal vault cytology (vault smears) is, however, recommended in certain circumstances: women who have had less than ten years routine cervical screening should have one vault cytology test and those who have CIN detected at surgery should have two, within 24 months of the operation. If all test results are negative, screening should cease permanently as there is no cervical tissue in which CIN can develop.[16] Undertaking vault cytology testing of asymptomatic women outside these guidelines is to screen for vaginal cancer, a very rare malignancy which does not fit the criteria for any organised screening programme.

It has been suggested that vaginal vault cytology is sometimes being undertaken inappropriately, outside the recommendations of national guidelines, which is wasteful of resources and potentially harmful to women.[30] There are also women for whom guidelines do not apply i.e. those who have a diagnosis of malignancy, where the specialist will dictate what they feel is the most appropriate follow-up on an individual patient basis. Women who have abnormal vault cytology are subsequently treated according to local protocols.

The existing literature concerning the indications for hysterectomy had not been updated for some time[1] and the literature concerning use of vaginal vault cytology in follow-up after surgery was sparse when this study was conceived. It was known that the great majority of women underwent hysterectomy for benign indications[1;2;162] and that vault cytology was a matter of some considerable debate.[24;27]

Current NHSCSP guidelines concerning vault cytology are based on expert opinion rather than gold standard research evidence; no randomised controlled trials have been undertaken. The majority of published literature suggests that follow-up by means of vault cytology has a limited place in follow-up of those cases where women had a hysterectomy which revealed invasive or pre-invasive disease.[71;91] However, following hysterectomy for benign disease, the value of vault cytology is unproven. [22;24;101]

This study aimed to establish which women were having hysterectomy operations, why and whether or not they subsequently had any vaginal vault cytology performed. The study objectives are given again in Figure 36.

Figure 36. Study objectives

Primary Objectives

- To estimate incidence rates for hysterectomy operations, in the West Midlands region of the UK
- To describe variations in incidence of hysterectomy and establish the factors associated with variability
- To describe the current indications for hysterectomy in West Midlands
- To describe cervical screening patterns prior to hysterectomy
- To establish the current pattern of follow-up after total hysterectomy by means of vaginal vault cytology test
- To describe the results of vaginal vault cytology with respect to histology at hysterectomy and establish the factors associated with having an abnormal result
- To assess if vaginal vault cytology is being undertaken appropriately and establish the factors associated with inappropriate usage

Secondary Objectives

- To provide high quality evidence to inform national guidelines.

7.2 STUDY LIMITATIONS AND PECULIARITIES

7.2.1 Justification for the study

To establish which women were having vaginal vault cytology and why, it was first necessary to establish which women were having hysterectomy operations. Establishing which operations were total or subtotal hysterectomies enabled classification of women according to who should continue with routine cervical cytology, who should have vault cytology and who should cease to be screened. Hence, the concepts underpinning this study: identifying a suitably large cohort of women who had a hysterectomy operation during a defined period, who could have their cervical and any subsequent vaginal vault cytology linked to their operative details so that patterns and trends could be established.

7.2.2 Limitations and usefulness of routinely collected data in linkage studies

Although increasingly common to undertake research using database linkage,[163] any study using routinely collected data is at risk of bias. The priorities for those responsible for recording the raw data will be different from those of the researcher, the measurements and standards are outside the control of the researcher and completeness of data may not be known.

To link datasets that were not designed for the purpose risks a significant loss of data where no reliable matching occurs or where items from one database are not able to be transferred to the other. The deliberate choice of NHS number, date of birth and UK postcode of residence in this study, was to utilise standardised, commonly recorded data, to facilitate optimal linkage. Studies of this nature have been conducted ever since healthcare data has been reliably stored electronically.[163;164]

The two key data sources are well established and respected. Hospital Episode Statistics (HES)[114] uses highly trained NHS Clinical Coders to upload data about every hospital admission or appointment, using a variety of internationally standardised coding systems to ensure that the data is of the highest possible quality.[110;116;117] National cervical cancer screening programme data is a very rich resource including data for the past 35 years, and its data entry and coding is regarded as being of 'high quality'.[111]

7.2.3 Use of confidential patient data without individual consent

The considerable ethical dilemmas that arose from using individual patient data without consent have been explored in Chapter 3. In essence, to conduct a database linkage study of this scale it was not practicable to obtain individual patient consent.

The potential benefit from the research for all women, outweighed any theoretical risk of harm to a few, by a transient breach in patient confidentiality for the purposes of linking data. A position that PIAG agreed with. As soon as the study data was linked and verified, and before any analysis took place, anonymity was restored: at first in part (pseudo anonymisation) and then, once hospital data had been obtained, full anonymisation with independent verification.

To protect against frivolous use of confidential patient data, there are many necessary approvals which any legitimate researcher must obtain before being granted access to such data. These processes, which were successfully navigated before the research could begin, ensured that the highest standards were applied and that the research concept had been independently verified by experts in the field of medical ethics.

At the time of study development and data collection the body responsible for overseeing this process of allowing researchers access to confidential data, without patient consent, was PIAG. However, subsequently PIAG has been subsumed into the National Information Governance Board (NIGB).[136]

Efforts were made to advertise the study in local research publications as suggested by PIAG. No-one came forward to ask that their details be removed from the study database and, as such, it is impossible to know if this was because the advertising did not reach the target audience or if it is because women were in complete agreement with the study aims and were happy for their data to be used.

Two lay persons were asked for their views during study development and their comments were integrated with the final protocol. It is plausible that the resulting study paperwork and patient information generated by their input was the reason why no women sought to have their data removed from the study database.

As patients were not approached for their individual consent, the study is completely inclusive and thus the findings should be generalisable. However, there is a valid argument that, had the opportunity presented itself explicitly, there were some women who may have chosen to be excluded from the study. These women may represent a discrete group for whom the normal 'medical model' of research and routine care does not apply. As we had no way of identifying those women, direct comparisons of the findings of this work against other research that has obtained patient consent, should be undertaken with caution.

The author of this thesis is a practising British doctor with enhanced Criminal Records Bureau clearance (CRB, an agency of the Home Office), employed by the NHS and funded by the NIHR to undertake this research in a well-respected academic institution.

It was suggested that the maze of approvals and permissions necessary for access to the patient data (outlined in Chapter 3) was disproportionate and potentially wasteful of resources. However, in view of subsequent national scandals concerning inappropriate use or loss of confidential data, it would appear that these were appropriate safeguards.[165]

The development of a unique study security policy (SLSP) was requested by the Security and Confidentiality Advisory Group (SCAG) of HES and its evolution involved close working with The University of Birmingham Caldicott Guardian. This was a productive relationship which led to several initiatives being adopted which have subsequently become established as 'good practice' for all research undertaken at The University of Birmingham: the use of removable hard drive storage devices which are smaller and easier to lock away than full personal computers; use of sophisticated encrypted removable storage when any sensitive material is to be transferred between computers and the principle that patient identifiable data should not leave the security restricted areas of the University.

Secure wiping of media that contained patient identifiable data has been undertaken and verified, as per study protocol and there have not been any security breaches throughout the study period. Other procedures i.e. 'disaster recovery' have, fortunately, not been required to date.

7.2.4 Use of local hospital histopathology records

Hospital's histopathology data had been intended to be merged with the main study database, on a large sample of the study population. This was to provide additional information, and to act as a cross-check of the quality of the coded data. However, the significant variability in the quality and quantity of the data from laboratories was a cause of considerable concern.

The need to ensure patient confidentiality and only use NHS numbers (a study requirement stipulated by PIAG) meant that there was no way of obtaining more specific data or of searching more rigorously at the laboratories. It transpired that, despite the intention that NHS number should be the key identifier for all patient records, some hospitals were still reliant on their own numbering or identification systems and as such their use of NHS number was erratic. Had the study been able to use patient name or other specific identifiers or been permitted to use date of birth and postcode (which were already available) then the usefulness of hospitals' data may have been amplified.

Additionally, various hospitals used several variations of diagnostic and histopathological coding, which were not comparable. It was reluctantly decided not to pursue this source of data as the results would have been of uncertain significance in the absence of independent validation.

Fortunately, the data received from HES and Exeter was of significantly higher quality than had been anticipated. Thus, if linkage had been undertaken on NHS number alone, just one automated search of Exeter data generated 5,754 records; a match of over 98% of those with NHS numbers and a match of over 93% of the whole study population. This was because NHS number was present in 95.4% (5,857) of the 6,168 HES records, which had already been validated to ensure all were legitimate.

This is a significant improvement over older data linkage studies[166] but is consistent with findings from a large-scale new project (The SAIL Databank) which has validated NHS number for use in multiple database linkages (specificity >99.8% and sensitivity >94.6%).[167]

The final Exeter dataset, after a significant amount of manual searching and postcode and date of birth electronic searches, actually included data on 6,065 women. The final merged dataset, after all duplications were identified and removed, included information on 6,141 women, of which 6,055 had NHS numbers.

7.2.5 The West Midlands as a choice of study population

The West Midlands region is regarded as a reasonable proxy for the whole of England and Wales, representing approximately 10% of the population in terms of numbers and having ethnic diversity second only to London. The region encompasses affluent and deprived wards and spans densely populated urban to isolated rural communities with a corresponding variety of hospitals. These facts, and the practicality of conducting the study local to The University of Birmingham, justified the choice of study population on more than just pragmatic grounds.

7.2.6 Data validation

It was a major undertaking to validate all the data received and re-code it to a standard that would permit statistical analysis. This was partly because of the large number of different data items that were available for the analysis and also because of the need to group codes into practical but clinically relevant sections. Early in the project, problems were encountered by the use of Microsoft Excel 2003®; this spreadsheet programme is limited to 65,536 rows of data and 256 columns. The number and complexity of the transformations required to generate the final study database necessitated use of a high specification personal computer, multiple files open in parallel and a double width monitor with additional laptop screen. Microsoft Access 2003® and SPSS® v15.1 software packages were also used at various stages in the validation and all the statistical analysis was ultimately undertaken in SPSS.

Methodical validation of data required a range of strategies including identifying missing and duplicated data, establishing validity of outlying values and consistency of information. In reality, the data obtained from Exeter and HES was of high quality. The few areas of concern were: recording of ethnicity, which was only present in two thirds of cases and some probable errors in recording the duration of hospital stay i.e. women discharged from hospital on the same day as they underwent major surgery, which would usually necessitate at least three or four days post operative recovery (HES data).

Hospital of treatment was another area of concern in the HES data: 121 operations were apparently conducted outside the region; most of these took place in counties bordering the West Midlands and may have reflected patient preference. Three hospitals, which are known to have departments of Obstetrics and Gynaecology, did not have any hysterectomy operations recorded during the one-year study period. There were, however, 712 operations conducted where no valid hospital code was recorded. Looking at the numbers of operations performed in the other hospitals, this was similar to the estimated numbers of cases in the 'missing three'. Crude postcode data supported this hypothesis, however, a decision was made not to 'assign' women to a given hospital but to just analyse the supplied information.

Exeter data was remarkably complete: only one woman, from 6,065, did not have an NHS number, all women had date of birth and a registered GP and only five did not have a valid UK postcode. For the 5,810 who had screening performed there was a date, test result and action code for each.

7.2.6 WMCIU coding algorithm of screening histories

The use of this Microsoft Access® visual basic programme, designed by the West Midlands Cancer Intelligence Unit (WMCIU) staff to classify women diagnosed with cancers into a screening history code, was a useful supplement to the study.

By modifying the algorithm, so that the date of surgery was substituted for the cancer diagnosis date, it then allocated women to a specific group representing all phases of their screening history. The resulting 238 codes, in the population of 6,141 women, were too extensive to permit meaningful comparisons. Thus, further subgroups were created, resulting in a final coding of 13 variants. The last screening test before surgery was the first discriminator (abnormal, normal, of uncertain significance or never tested) followed by the four main patterns of prior screening history (all normal, some abnormal, only one test ever or previous results of uncertain significance).

There were some assumptions in the programming which were not relevant to our study population (i.e. women over the age of 65 were usually excluded and tests taken in hospital or the private sector disregarded), allocation to the 13 sub-groups serve to counter-balance these.

7.2.8 Data coding and reclassification

A variety of coding schemes were used by HES and Exeter to permit comparison of their data with that from other sources, some international coding (i.e. ICD10), some national (OPCS4) and some unique to that database. Recoding some of these data was essential to permit appropriate comparisons.

7.3 DISCUSSION OF RESULTS

7.3.1 Demographic composition of the study population: which women had hysterectomy operations?

Incidence of hysterectomy

The 6,141 women included in this study were resident in the West Midlands region and all underwent a hysterectomy operation between 1st April 2002 and 31st March 2003. This equated to an annual, crude incidence of hysterectomy of 23 per 10,000 women, thus the 'average GP' surgery of 6,000 patients would have approximately seven women each year undergoing this major operation.[168]

Compared with the published literature this confirms that hysterectomy is declining in popularity, indeed there has been a halving in the number recorded annually in England over the past decade.[5;126]

Age

The study population were of a very wide age range; the youngest was only aged 17 years at the time of her obstetric hysterectomy, having had a normal vaginal delivery, but subsequent uncontrolled post-partum haemorrhage necessitated an emergency hysterectomy (suggested by HES coding). The eldest was 94 years at the time of surgery; she underwent a vaginal hysterectomy for repair of a vaginal prolapse.

The distribution of age was slightly skewed to the right, with a median age of surgery of 48.38 years but a mean of 51.12. This is consistent with the 'perimenopause' stage of a woman's life when menstrual difficulties are commonplace, but is somewhat older than in the last reported major review of hysterectomy in the UK (operations in 1994-95) where the median age was 45 years, although that study excluded cases of malignancy which may have increased our observed mean age.[1] Also, this finding of increased mean age is compatible with the observed reduction in the numbers of operations performed over time, as the introduction of less invasive techniques for managing menstrual problems are likely to have the greatest application and benefit for women prior to their menopause transition.

Age specific incidence rates for surgery varied widely with peak of 63 per 10,000 women per annum, in the 45-49 year age group but very low rates in women under 30. In women aged 80-84 years the rate was 14 per 10,000 demonstrating that age is no barrier to surgery in otherwise healthy individuals. Age standardisation of the study population did not make any meaningful difference to the incidence of hysterectomy and so crude rates were used throughout.

Deprivation

The study population was significantly more deprived than the population of England ($p=<0.001$) with 27% of the study population in the most deprived quintile and 14% in the least deprived.

However, deprivation of the study population was not significantly different from that of the West Midlands region, i.e. the women represented the full range of deprivation quintiles in approximately the same distribution as the general population of the area from which then came.

The finding fits with from those of previous studies of the epidemiology of hysterectomy, where higher rates of surgery have been noted in women of lower social class.[2] In the most recent cohort study it was suggested that women having higher levels of academic attainment are significantly less likely to have a hysterectomy than those with few qualifications.[12] It is timely to acknowledge that, when compared with England as a whole, the West Midlands contain more areas of significant deprivation and as such, although there are many advantages in using this region, the study population cannot be entirely representative of the UK and thus the reader needs to be cognisant of this.

Age standardisation of the deprivation data confirmed that, even accounting for the fact that younger women were more likely to be in the lower deprivation quintiles[169], the observed differences in hysterectomy incidence were true with a range for 25 per 10,000 in quintile one to 20 per 10,000 in quintile five ($p=0.001$).

Ethnicity

The ethnic make-up of the study population, where this data was recorded, was significantly different from the background population: although the proportion of white British was similar; women from Afro-Caribbean groups were over represented with women from Asian backgrounds being under represented. This may be due to the fact that Afro-Caribbean women are more prone to significant fibroid disease with rates of up to 9x those in the general population.[170]

Hysterectomy incidence was calculated for the main ethnic groups, age standardisation making little difference. The crude rates ranged from 23 per 10,000 in White women to 33 per 10,000 in Black women, numbers of Chinese, mixed and other races were too small to allow for meaningful comment.

As ethnicity was recorded for only two thirds of the study population some caution should be taken when interpreting and extrapolating these findings.

Duration of hospital stay

The mean duration of hospital stay was five days, (mode = four days); consistent with findings of previous studies[1] and fits with normal practice in that women who undergo routine hysterectomy surgery without complication are usually discharged on the fourth day. There is the inevitable skew to the right as some women had complications and complex surgery, in addition to having underlying general medical problems, and may have required a far greater duration of admission.

The maximum hospital stay was 81 days post operatively. However, 107 women were coded as being discharged on the same day as their surgery. This was not related to transfer to another hospital and probably represents miscoding; the impact of this on the overall findings is likely to have been very small. Within two days of surgery 228 had left hospital, ethnicity was recorded on just 47% of these, but the data suggested that Asian and Black women may be over represented in the 'early discharge' group. The diagnosis for these 'early leavers' covered the whole range with 15 malignancies represented.

Destination on discharge from hospital

On leaving hospital the vast majority of women went 'home' (98.14%). Ten were noted as having died in hospital and a small number were transferred to other types of accommodation including one who went to prison to recuperate.

Deaths in hospital

Ten post operative deaths was higher than would have been anticipated using recognised complications rates[1] for hysterectomy and giving a mortality rate of 1.6 per 1,000 hysterectomy, or 0.16%, of the study population. However, previous studies excluded women with malignancy and half of the deaths were in cancer patients (four of the five having disseminated disease).

When split by underlying diagnosis the mortality rates became 7 per 1,000 for hysterectomy in cases of malignancy and 1 per 1,000 for benign indications. Two of the 'benign' cases had very little data recorded and it is possible that their discharge destination was miscoded which may have reduce the mortality rate further.

Death is a rare outcome and this study was never powered to look at it in any detail but the observation does bear further investigation. The Royal College of Obstetricians and Gynaecologists publishes guidance information for clinicians to use when obtaining informed consent from women prior to surgery; this states that there is an operative mortality of one in 4,000 cases. Even if these are just applicable to hysterectomy for benign indications these study findings are four times worse and should prompt an appraisal of the current situation.

7.3.2 Cervical screening history preoperatively: why these women may have had surgery

Overview

The 6,141 women underwent 36,151 cytology tests between them, of which 34,174 were prior to surgery and 1,977 after surgery. In those women who had a sub total hysterectomy post operative tests were still cervical screening, but most were vaginal vault cytology tests.

Index test

The index test was defined as the last cervical screening test prior to surgery, thus it usually took place within five years of the operation date. It was examined in some detail because it is plausible that the test result may have had a bearing on the decision to proceed to surgery: 83.8% of index tests were essentially 'normal' results, which compares closely with the likelihood of having a normal test at any screening point in 2002-03.[171]

Only 18 women were noted to have invasive disease at their index tests and dyskaryosis was detected in 161 women. In 297 (4.84%) cases the result was borderline or some another result of uncertain significance, which is a little higher than the normal population.[171] Having an abnormal index test result was associated with greater levels of deprivation, this is consistent with the known risk factors for CIN and cervical cancer.[66]

There was no cytology testing prior to surgery on 354 women; these were more likely to be aged over 70. This observation is compatible with the introduction of national screening in 1984, as this population of women would have been aged at least 50 and as such were a low priority. No woman is compelled to have cervical screening and some women consistently exercise their right to opt-out of the national programme. All women aged under 20 and over 90 years had not had any cervical screening prior to their hysterectomy, which is entirely consistent with national screening guidelines.[16]

When considering the result of the index test only 2.7% were classified as inadequate; the national average figures for inadequate rates in 2002 were 9.4%, thus the study figure was significantly lower.[15] It is possible that some women had a previously inadequate test repeated prior to surgery to reduce the risk of missing potential cervical disease. Alternatively, as these women would have been seen in a gynaecology outpatient clinic prior to surgery their index test may have been performed by a gynaecologist under optimum conditions (i.e. properly trained and appropriately equipped).

Since the introduction of liquid based cytology techniques throughout the UK inadequate rates have subsequently fallen and in 2007-08 the national level stood at just 2.9%.[15]

Women who had an index screening result of dyskaryosis' were generally younger than those having had completely 'normal' or severely 'abnormal' results. This finding is consistent with the natural history of cervical cancer, in that the changes of cervical intraepithelial neoplasia (CIN) take many years to develop into invasive cancer and pass through defined stages which may spontaneously regress, thus, cancers typically occur in older women with pre-invasive changes being detected earlier.[2]

Observed screening compared with anticipated screening

An attempt was made to estimate how many cervical screening tests women were likely to have undergone at any given age, to permit comparison with the actual data. This estimation was a combination of several factors: firstly, the known screening guidelines that were in place at the time of the testing[16]; the known introduction of the national cervical screening programme (NHSCSP) and the fact that when pregnant and in the months subsequent to childbirth, cervical screening is not recommended.

The estimates were generated completely separately from the study data but, when compared, showed a similar distribution of frequency (Chapter 6, figure 9) and an almost identical total number of tests undertaken. However, women in the study had more screening tests at a younger age that the estimated model. This is consistent with them having additional pathology compared with 'normal' women of a given age.

White and Asian women typically had more cervical screening than women from other ethnic backgrounds ($p=<0.001$), however, even with the large study numbers the significance of this finding is uncertain as the rate of ethnicity recording was sub-optimal. Deprivation did not have a clinically significant impact on pre-operative screening in this population of women, although a negative correlation was observed (increased deprivation associated with less screening).

Entire preoperative screening history and the WMCIU algorithm

As outlined in sections 4.4 and 5.5.4.4, women's entire screening history was summarised using a modified version of an algorithm developed and used by the WMCIU. The additional value of this coding is that any future work resulting from this study can use the same groupings to facilitate comparisons.

The complex original coding was simplified into 13 groups for analysis. Women, who had not ever undergone any cytology testing, were noted to be significantly older at the time of hysterectomy than all other women. This may be because they presented late (i.e. the type of women who avoid any contact with healthcare personnel unless absolutely essential). These unscreened women were also more likely to be from an ethnic grouping other than White British, which is consistent with findings of other studies[169;172] and it is plausible that other barriers to access to healthcare may have accounted for their delay in having surgery (i.e. language or cultural factors), but this study was not able to investigate these further.

Of note, 45.9% of women always had completely normal cervical screening results, 6.19% never had any cervical screening but 9.85% had abnormal cytology prior to surgery. Younger women and those living in more deprived areas were most likely to have ever had an abnormal cervical screening test results.[66]

7.3.3 Outcome of surgery: which operation and what diagnosis?

Hospital of surgery

There were 16 hospitals in the West Midlands region which represented 86.64% of the study population: median age at surgery varied from 47 to 50 years, a small difference. Ethnicity and deprivation, however, varied widely across the region.

A key finding was the significant variability in coding of ethnicity data between hospitals. Several recorded ethnicity for over 90% of their hysterectomy patients; however, three hospitals recorded it in less than 40% of women. In one hospital there was a clear indication that miscoding was occurring as there were no 'white' women documented, as this hospital represented over 10% of the study population this may have had a bearing on the distribution across ethnic groups as invariably the largest proportion would have been white.

The plan to use hospital histopathology laboratory data to supplement the main study database had to be abandoned, as outlined in sections 3.4.2 and 4.6, thus was disappointing but served to highlight the major disadvantages of data linkage studies and contextualised the difficulties that the NHS is currently having in drawing together all its various information technology resources.[173]

Operation type

Operation specific OPCS codes were used to divide women according to the type of hysterectomy operation, i.e. total or sub-total. A very small number (n=8, 0.13%) could not have this information established, even from close scrutiny of their HES records as the only code applied was a non-specific 'hysterectomy' code and no other code was present to confirm the presence of the cervix uteri in the pathology specimen. All vaginal hysterectomies were assumed to be total as it is not possible to remove the body of the uterus vaginally without also removing the cervix.

92.77% of operations were coded as total hysterectomies, fewer than had been anticipated from the UK literature, where rates of over 97% had previously been noted.[1;2] Women having a total hysterectomy were a little older than those undergoing the sub-total variant (median: 48.88 vs. 45.16yrs, $p<0.001$) and were slightly more likely to be of White ethnicity than Black or Chinese, although numbers were small.

There was no association with operation type and duration of post operative stay, with both groups having a median stay of 5 days after surgery which is consistent with the literature.[1] There was no association detected between deprivation status and operation type, thus no suggestion that women from different backgrounds are receiving different standards of service from the NHS.

Final diagnosis at surgery

The diagnosis at the time of hysterectomy was established using ICD10 codes. For each woman the 'worst' of all codes was selected as the main diagnosis, this was then compared with the result of the index test and if the index result was significantly worse than the hospital diagnosis then the index result took precedence. This was because it was possible that colposcopic treatment had occurred between hysterectomy and index test, thus treating the significant abnormality that would, otherwise have been removed at hysterectomy. Only 28 women had their final diagnosis changed this way and thus even if this additional cross-checking had not been undertaken there would have been little change in the study findings.

A malignancy was recorded in 11.61% of the study population; higher than had been anticipated. However, this also included non-gynaecological disease and may reflect the overall trend for using less invasive treatments for managing benign conditions. Intraepithelial neoplasia or carcinoma-in-situ was present in 3.00%; somewhat lower than had been anticipated (see sample size calculations Chapter 3.5.1), which may represent success of colposcopy clinic excision. The vast majority of women (82.90%) had benign diagnoses and a further 2.51% could not be classified into a meaningful diagnostic category.

The three main diagnosis groups were compared and, as anticipated, women with a cancer diagnosis were older than the other groups. Most gynaecological cancers increase in incidence with increasing age, in particular, endometrial and ovarian cancer tend to present after the menopause, and squamous cervical cancer usually takes several decades to develop.[174]

The intraepithelial neoplasia group was younger than the larger group of women who had benign disease. This may be because the benign group would include older women who would be having hysterectomy surgery as treatment for prolapse and peri-menopausal vaginal bleeding concerns, whereas women having a diagnosis of CIN are likely to have been detected by routine cervical screening.

There were no clear associations detected between deprivation or ethnicity and diagnostic category, as small numbers made it difficult to make meaningful comparisons. However, it did appear that white women may be more likely to have a malignancy than the other groups. Women with cancer diagnoses tended to stay in hospital longer than the other groups (median 6 compared with 4 days). This was not unexpected as surgery to remove a known or suspected cancer is usually more extensive or 'radical' than routine surgery.

The last cervical cytology test before surgery (the index test) was compared with the overall diagnosis as it had been postulated that women having had abnormal cytology would be more likely to have hysterectomy operations for non-benign reasons.

Whilst there was a very clear association between having an abnormal index result and having a hysterectomy for non benign indications (Pearson $\chi 2$ = 1,612.528, p=<0.001) the level of disagreement between them was also significant (McNemar = 433.246, p=<0.001), thus although related, the index test result is not suitable as a predictor of future surgical diagnosis.

Full screening history was also compared with the final diagnosis. Again, there were clear associations detected, with women who had never been tested or having only had one pre-operative screening test being more likely to have a cancer diagnosis. It is possible that these were women who may have actively avoided attending for screening until presenting with symptoms.[81] It is known that 50% of cervical cancer cases in the UK occur in women who have never attended for routine cervical screening.[151] Conversely, women who had several abnormal cytology tests were more also more likely to have CIN or carcinoma in situ at surgery.

There was no clear association noted between operation type and final diagnosis. It had been postulated that women with a cancer diagnosis would be very unlikely to have subtotal surgery as the objective would usually be full clearance of disease and staging, but this hypothesis was not proven.

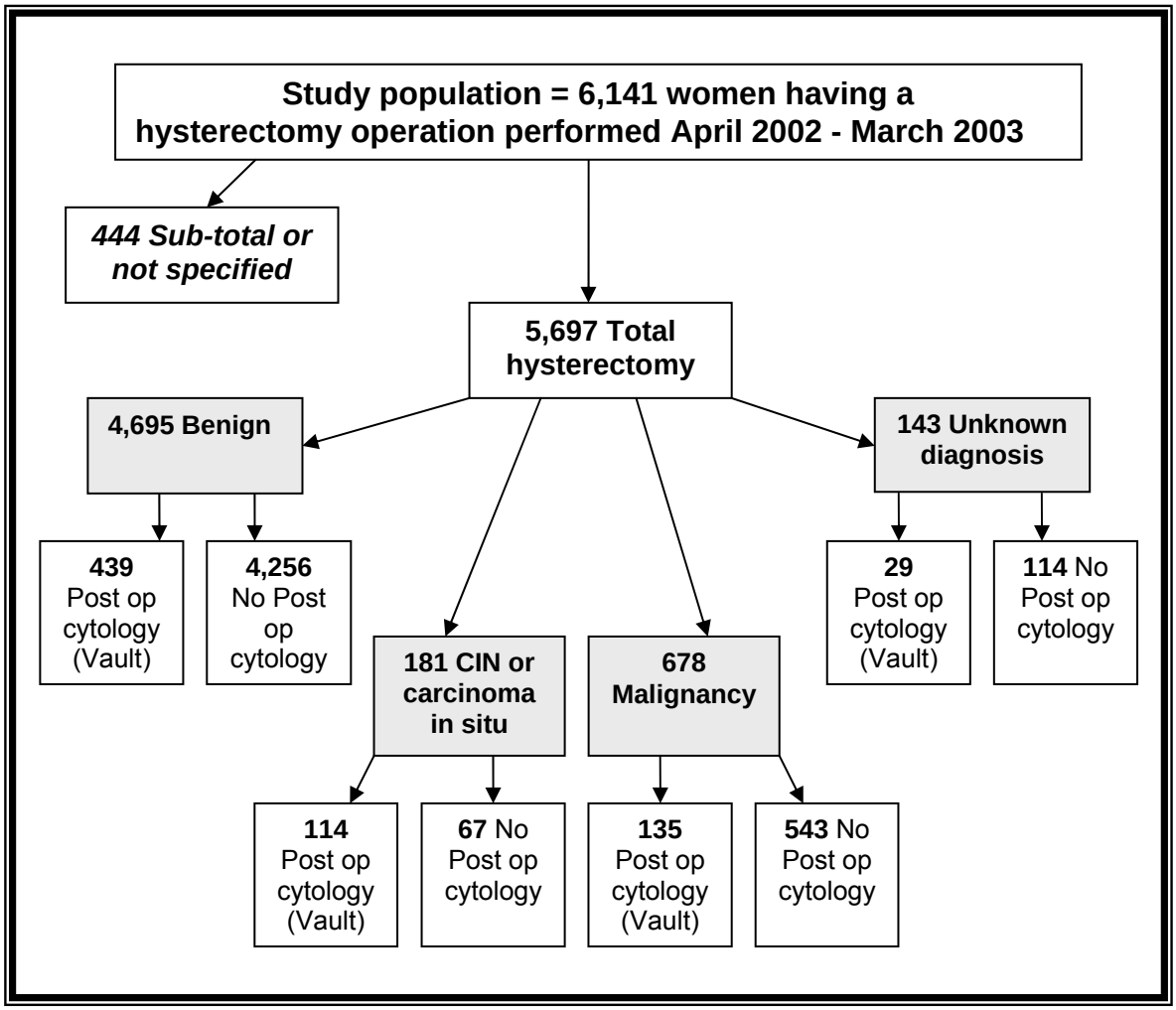
Multiple regression analysis was used to establish if there were any pre-operative 'patient' factors associated with an increased likelihood of having a total rather than a sub-total hysterectomy: several factors were included in the model (age, deprivation, index test result) and both age and an abnormal index test result were found to be positively associated. However, the various associations only accounted for 3% of the total and as such they do not have a meaningful bearing on the outcome. Thus, there must be other factors at work; patient factors (i.e. presence of concomitant disease or patient preference) or doctor related factors (i.e. individual surgeon's preference, expertise, staffing etc.) that could not be established from this type of research project.

7.3.4 Follow-up after surgery by means of vaginal vault cytology tests: which women are tested?

7.3.4.1 Overview of women having vault cytology

One of the key study objectives was to establish which women are having post operative vaginal vault cytology testing (vault smear tests). The flowchart, Figure 37 (an abridged version of the one in section 6.4), illustrates the numbers of women in the various groups.

Figure 37. Study participants, operation type and use of vault cytology



The main sub-group of interest within this study were women having a total hysterectomy (n=5,697) and the numbers were large enough to permit meaningful comparisons. Having sorted the data into operation type (total or subtotal) and the various diagnostic groups and presence or absence of post operative cytology, it was finally possible to establish which women were followed up by vault cytology and to allocate a coding based on how appropriate this follow-up was, according to national guidelines.

This ‘appropriateness coding’, based on national guidelines where they existed, factored in changes to the guidance over time. In-depth inspection of the numbers; was undertaken; of particular note, only 13 of 181 women with CIN at surgery had follow-up exactly according to guidelines (two vault tests within two years of surgery), a further 11 had testing but results were abnormal and so correct screening interval could not be assessed.

For statistical analysis a more simplistic approach was taken using the premise that national guidelines are correct and that follow-up after hysterectomy for benign reasons is never indicated, whereas follow-up after hysterectomy for CIN should be performed. Guidelines that were released after the data collection period of this research, suggest that women who have had less than ten years of routine cytology prior to undergoing a total hysterectomy should have one vault cytology test post-operatively. However, as this change was introduced in 2006 it was deliberately not factored into the main analysis, but was considered briefly.

Another change introduced in 2006 was that follow-up after CIN should comprise two tests within two years of surgery where the disease was completely excised (assuming all results normal), whereas previously the guidelines had stated two tests within 18-months of surgery. A decision was taken to consider vault cytology within 24-months of surgery as being done according to guidelines; this was intended be inclusive and reasonable.

If CIN is detected in the margins of a hysterectomy specimen, then screening should continue.[16] Our data did not reveal the detail of disease-free margins in histopathological specimens and it was not factored into the analysis. Had the hospital histopathology data been more useful then this may have provided data on disease-free margins.

Coding the 'appropriateness' of vault cytology could not be applied to women who had a total hysterectomy for malignancy as there were no national guidelines to be applied. Follow-up is currently left to the discretion of the surgeon responsible for the surgery and often involves colposcopic examination of the vagina, with vault cytology and/or guided biopsy of suspicious lesions. From these findings it would appear that there is no local consensus or recommended standard on follow-up after gynaecological malignancy as, for these 678 women with a cancer diagnosis, just 20.50% were followed up by vault cytology (n=139) compared to 62.98% of women who had CIN.

7.3.4.2 Demographic factors

The demographic characteristics of women who had any post operative testing performed were compared with those who did not and several differences were detected: Women having any post operative cytology tended to be younger, less deprived, non-white and have a shorter duration of post operative stay than those who were not tested.

As these findings were somewhat surprising, the subgroup of just those women who had a total hysterectomy was selected as this was a more appropriate group of women who may be eligible for vault cytology and the analysis re-run. Again all the observations held true: non-white, less deprived, younger women who stayed in hospital for less time, than their counterparts, were more likely to have vaginal vault cytology testing (all p=<0.001).

The reasons for these findings may be complex. It is plausible, but not proven, that women who are less deprived may be more assertive in their requests for follow-up testing. Certainly, screening uptake is higher in this population routinely so this observation may just reflect the underlying phenomenon. The increased use of vault cytology in non-white women is less explicable as these women are known to be less inclined to participate in all screening programmes.[175;176]

The association with shorter hospital stay and vault cytology was surprising, one would anticipate that the need for screening would be associated with worsening pathology and worse prognosis which are both known to be related to increased duration of hospital stay.

The finding that younger women are more likely to have post-operative screening is less surprising, as there have been high level discussions, nationally and internationally, concerning the appropriate role for cervical screening in younger women.

Following the year of this study, a new guideline was released suggesting that women who had less than ten years screening prior to hysterectomy should have one vault test post operatively. Thus, it is plausible that this recommendation was being implemented ad hoc, particularly by some well informed hospital clinicians, prior to national roll-out.

7.3.4.3 Pre-operative screening history

It was postulated that women who had abnormal index cytology tests could be more likely to have vault cytology undertaken, irrespective of their final operative diagnosis. Analysis confirmed this with Pearsons χ^2=345.399 (p=<0.001). Women's entire screening history was then compared with vault cytology status and again strong associations were detected: Pearsons χ^2=369.972 (p=<0.001). Thus, women with entirely normal pre-operative cytology or women who never had any pre-operative testing were highly unlikely to be screened post operatively, whereas those who had some abnormal screening results were more likely to have vault cytology undertaken.

When patterns of entire screening histories were compared with each other, several differences were observed: women who had ever received an abnormal cervical cytology result were significantly more likely to have post operative vault cytology than women who only had normal cervical screening results, Pearsons χ^2=224.024, (p=<0.001). These findings are all consistent with clinicians attempting to follow screening guidelines.

7.3.4.4 Diagnosis at time of surgery

When final diagnosis at time of surgery was compared with the likelihood of having a vault cytology test a very strong association was detected; Pearsons χ^2=503.311 (p=<0.001). This finding was anticipated because national guidelines suggest a place for vault cytology following total hysterectomy for CIN. However, this was the only recommended use for vaginal vault cytology in the UK at the time of the study.

Thus, it was anticipated that the great majority of women having CIN at hysterectomy (n=181) would have at least two vault cytology tests done within two years of surgery. However, only 114 (62.98%) of these women ever had any vault cytology within four years of surgery, and of these, only 13 (7.18%) had screening done precisely 'to protocol' (defined as 2 tests within 2 years, both results normal): 50 women (27.62%) had too many tests performed, 16 (8.84%) had testing done but later than the recommended interval and 11 had abnormal findings at vault testing and so guidelines ceased to apply.

It is possible that other 'factors' had a greater influence on likelihood of adherence to national guidelines and that the scope of this research did not cover them. Alternatively it may be that these women were having colposcopic assessment and vaginal biopsy rather than cytology testing.

Overall these findings were disappointing. Of the group of women who were definitely eligible for vault cytology post operatively, although over 60% were screened, very few were screened according to national guidelines (per protocol). The very large group of women who had a benign diagnosis at surgery included over 9% who had at least one subsequent vault cytology test. This would suggest significant waste, both in terms of the emotional cost of undergoing screening[17] and also financial cost to the NHS. These observations are consistent with previously completed audit work by the author[28] and confirm that there are ongoing problems with inappropriate over-use and under-use of vault cytology testing.

It is not uncommon for guidelines to fail in practice[177;178] however there are a range of evidence based, established strategies that may be adopted to maximise adoption of best practice.[106;179] The guidelines for use of vault cytology are complex[84] and changes introduced in 2004 were not disseminated effectively throughout the UK, thus it should not be surprising that they are not being adhered to.

7.3.4.5 Patient factors associated with having vault cytology

Multiple logistic regression analysis was undertaken in an attempt to establish which of the 'patient factors' had a significant bearing on whether or not a woman who had a total hysterectomy subsequently underwent any vault cytology screening. Younger age, less deprivation (lower IMD07 score), operative diagnosis (CIN or cancer) and abnormal result of the index test were all significantly associated with an increased likelihood of a woman subsequently having vault cytology.

Some of these findings had been anticipated i.e. result at operative diagnosis and index test result. However, age and deprivation were somewhat surprising, although the odds ratios for these (age = 0.982, deprivation = 1.019) indicate that although potentially 'significant' in statistical terms, in reality their impact will be very small as their usefulness in clinical practice is doubtful.

To explore possible 'external' factors influencing the likelihood of a woman having vault cytology, the hospital of the surgery was investigated and a clear association was detected (Pearson χ^2=159.224 (15df, p=<0.001). The percentage of women at each hospital subsequently having vault cytology ranged from 5.1% in a small hospital (137 hysterectomy operations in one year) to 25.7% in a large tertiary centre which would be anticipated to deal with a higher proportion of malignancies.

However, there were several gaps in the hospitals data, with three major hospitals in the area not having any women coded as having had surgery there, which was probably a coding mismatch at HES. Other women had surgery performed outside the West Midlands region or had invalid hospital codes. There were too many institutions to permit the use of logistic regression analysis effectively and as such this is an area that may benefit from further research.

7.3.4.6 Factors associated with adherence to national screening guidelines

In addition to establishing which women are having any vault cytology testing it was essential, for the study aims, to establish if national screening guidelines were being followed closely (adherence) and if the vault testing that took place was occurring according to protocol (appropriateness).

National guidelines[16] apply to those women having had a total hysterectomy for benign disease or for CIN, and where their test results are always normal the guidelines are clear and these two groups were explored. However, if abnormalities are detected at vault testing the guidelines are not specific about the next steps that should be taken. Thus, in the analysis, an uncertain classification was used for women who had post operative vault cytology where the results were inadequate, borderline or confusing or where guidelines could not be applied. Additionally, there are no national guidelines concerning follow-up after malignant disease with vault cytology and so an assessment of appropriateness in these cases could not be made.

National guidelines have been modified since the data collection period of this study (2004).[89] Thus the decision as to whether or not a woman had been screened 'appropriately' was based on the guidelines that were in place at the time of hysterectomy and the two subsequent years, rather that those currently in use. However, even if the analysis had been based on the latest guidelines there would have been little impact on the overall findings:

1. Follow-up after hysterectomy with diagnosis of CIN

Logistic regression analysis was undertaken and suggested that only the presence of an abnormal index test prior to hysterectomy was a statistically important predictor of having appropriate vault cytology testing and even this only made a very small difference, odds ratio of 3.14 but Nagelkerke R^2 = 0.11 and a final fitted model of 67.6% with the starting point of 64.8%.

2. Follow-up after hysterectomy with benign diagnosis

Following hysterectomy for benign disease, guidelines explicitly specify that vault cytology is not indicated. However, of those women who had a total hysterectomy with benign results (n=4,695), 439 went on to have subsequent testing (9.35%). The overwhelming majority of these tested women (n=376 from 439) only ever had negative vault cytology, of these 23 had more than two tests taken.

Logistic regression analysis was then run on just those women who had inappropriate vault cytology performed and it revealed several factors to be related to an increased likelihood of inappropriate use: younger age, higher deprivation score (thus being less deprived), and the presence of an abnormal index test result, despite having benign diagnosis at surgery. However, only the presence of an abnormal index test result had an odds ratio of greater then 1.5 and with Nagelkerke R^2 = 0.048 and a final fitted model of 90.3% but unchanged from the starting point, thus the clinical significance and application of these findings is questionable. There are clearly other non-patient factors at work which this study was not designed to explore.

7.3.4.7 Factors associated with having an abnormal vault cytology test result

To establish the true value of vault cytology and make recommendations about its usefulness, it was important to distinguish between those women having normal and abnormal vault test results.

Less than 3% of the vault tests returned an abnormal result; these were not related to age, deprivation, ethnicity or duration of hospital stay. The only notable association was between the main operative diagnosis with those women who had cancers or CIN being more likely to return an abnormal vault cytology test result than women having a benign diagnosis ($p=<0.001$). Thus current national guidelines, which target women who had CIN at hysterectomy, are supported by these findings. This is the first UK study to establish this association.

For women who had benign disease at hysterectomy and who had vault cytology (439), six had at least one abnormal vault test result (1.37%), however, 57 (12.98%) had results of uncertain significance. Unlike those women with normal results where most only had the one test done, 46 of the women with 'uncertain' results had further testing done.

The women who underwent a hysterectomy for malignant indications did not have any applicable national guidelines concerning their follow-up. Thus, it was the responsibility of their consultant to determine whether or not vault cytology should be undertaken.

This study was not powered to look at cancer cases, however observations were made: of the 135 women followed-up after a cancer was detected at surgery, only two (1.48%) had clearly abnormal results, 33 (24.44%) had results of uncertain significance and the great majority (74.07%) only ever had normal results.

Without access to reliably linked hospital data it is not possible to assess the accuracy of the vault cytology findings, however, the increasing presence of results of uncertain significance with worsening diagnosis does bear further investigation.

The systematic review undertaken by the author[24] concluded that there is no demonstrable benefit in screening after hysterectomy for benign disease, the findings of this study support this, with very low rates of disease detection in those screened. However in the absence of histopathology laboratory data or a case notes review to verify these results, some uncertainty remains. The systematic review suggested that there is no evidence to suggest changing guidelines with respect to screening after CIN I/II, this study confirms this assertion as there were more abnormalities detected in this population.

7.4 SUMMARY OF STUDY FINDINGS

Thus, this study has demonstrated that hysterectomy is still undertaken frequently and is not limited to certain ethnic groups. There is no apparent age limit applied to women being able to undergo this major operation, although the 40-60 years range remains the most likely time for surgery, corresponding with the climacteric stage in a woman's life.

There was a clear association between hysterectomy and social disadvantage in England, with a significantly higher hysterectomy rate in those women living in more deprived areas.

All major surgery carries risk; the in-patient death rate within this population was 1 per 1,000 women having surgery for benign indications and 7 per 1,000 for women having malignant disease. These are higher than current published RCOG figures.

The great majority of women who have a hysterectomy will have had cervical screening at some time prior to surgery; usually they will have had more screening tests performed than the general population at any given age. Younger women and those from White and Asian backgrounds had more testing that those from other ethnic backgrounds. Younger women and those from more deprived areas were most likely to have had a history of abnormal cervical cytology.

Hysterectomy is known to be routinely carried out at 19 different hospitals across the West Midlands; individual surgeons ranged from performing just one or two procedures to over 150 procedures annually. Sub-total hysterectomy was performed in over 7% of operations, significantly more than previous studies have shown, thus it would appear that this variant is being used more frequently. Sub-total surgery was used in younger women of Black or Chinese origin more frequently than in White women, however, there were no other associations with operation type. Duration of post operative stay was not associated with operation variant.

A malignancy was found in 11.61% of the study cohort, a higher proportion than was anticipated. This may reflect an overall decrease in use of hysterectomy as a treatment for benign conditions, rather than a real increase in cases of malignant disease. Malignancies tended to be found in older women, with CIN being found in the younger women; consistent with the natural history of these diseases. Diagnosis was not associated with deprivation or ethnicity.

Logistic regression analysis of the factors associated with use of vault cytology post hysterectomy confirmed that post-operative vaginal vault cytology testing was undertaken more frequently in non-white, less deprived, younger women who stayed in hospital for a shorter period than their counterparts. The reasons for these findings may be complex and require further research to understand and confirm.

Of the women eligible for vault cytology according to national guidelines, although over 60% are screened at some point, very few are screened exactly according to the specified protocol.

A substantial minority of women who underwent a total hysterectomy for benign indications had vault cytology tests performed (9.35%, n=439), confirming that there is widespread inappropriate use of this test. Women followed-up after malignant disease do not usually have vault cytology testing performed, but there is wide variation between hospitals with a range of 4.9 to 25.7% being followed up in this way. This may reflect the lack of national guidelines or disagreement between specialists as to the value of the test.

Logistic regression analysis of the factors associated with adherence to national guidelines, concerning vault cytology post hysterectomy for CIN, revealed that it is only the presence of an abnormal cervical screening test prior to surgery (the index test) that really influences this behaviour. In women who had benign disease, inappropriate use of vault testing was more common in younger, less deprived women, in addition to those having had an abnormal index test result. Non-adherence to national guidelines is of concern but is consistent with findings from other research.[106]

Women who had CIN at surgery did appear more likely to have abnormal vault cytology results than those having benign diagnoses, suggesting that the national guidelines are targeting the right women.

7.5 RECOMMENDATIONS

The findings of this study suggest that further research needs to be undertaken in several areas of uncertainty:

Investigation into the accuracy of data concerning the ethnic distribution of hysterectomy could be explored by looking at more recent cohorts of HES data and linking it with one of the Primary Care databases which now routinely code ethnicity data.[112]

Hospital's histopathology laboratory data should provide a rich source of research information if it can be linked with other electronic databases, if permission can be granted to use other patient identifiers this should be revisited. When hospitals throughout the NHS embrace NHS number and standardise their coding of samples, this type of research could be undertaken successfully and in future will provide valuable comparisons for assessing the validity of HES and Exeter data recording.

The demographic data presented has identified variability in the type of women having hysterectomy operations (deprivation and ethnicity). Thus a larger scale study just considering HES data, perhaps spanning several years of data for the whole of the UK, would provide a rich data source and would confirm or refute these new observations.

Use of the WMCIU algorithm provided a standardised way of categorising women's entire cervical screening history and it is suggested that this software should be used in future work of this nature: this will allow for close analysis of cases and permit comparisons. Further work, considering in some detail the cancer cases detected within this cohort, and using the algorithm, may generate valuable new associations for gynaecological and other malignancies in women.

The unexpected finding that over 7% of hysterectomy operations leave some or all of the cervix in-situ deserves further investigation. Thus a larger, more up to date, anonymous HES cohort could be identified (i.e. all of England) to see if this is a real change in practice and then look for confirmation of the associations with age and deprivation. Additionally diagnosis should be investigated to see if this is related to having sub-total surgery. With an increasingly obese society it is possible that physical patient factors could be a cause of the increase i.e. it is technically challenging and can prolong surgery to remove the cervix at the time of an abdominal hysterectomy in a very large patient. To investigate this hypothesis it would be necessary to link HES data for sub-total hysterectomies with one of the primary care research databases.

The finding of a higher rate of in-patient deaths than the published figures is a cause for concern and deserves urgent investigation. To do this a further, up to date, large HES extract would need to be obtained but this time data concerning deaths could be requested from the General Register Office of the Home Office, based at

Southport, Liverpool. Additionally a case-notes review of these cases could provide valuable data and identify the highest risk cases.

Further research needs to be undertaken to examine the reasons why less deprived, younger women are more likely to have vaginal vault cytology post-hysterectomy. Additionally, it would be helpful to establish if there are any individual surgeon or hospital specific factors at work in determining which women undergo vault cytology and how appropriate this is.

Having an abnormal vault cytology test result appears to be associated with worsening diagnosis at hysterectomy. This result is intuitively correct but few studies have examined this subject in the past 15 years and as such ongoing audit of vault cytology will be helpful in confirming or refuting the findings of this study.

Finally, it would appear that there is considerable confusion over the use of vaginal vault cytology testing and there is an argument that, where such uncertainty exists, the clinician responsible for the hysterectomy should have responsibility for any ongoing follow-up and thus vault cytology testing should become a secondary care initiated investigation, if it is used at all.

CHAPTER EIGHT: CONCLUSIONS

INTRODUCTION TO CHAPTER

This concluding chapter summarises the important study findings whilst reminding the reader of the limitations and generalisability of this study then finally making recommendations for clinical practice and future research opportunities.

8.1 SUMMARY OF FINDINGS

Removal of the uterus is an operation that has been remarkably successful as a means of managing a diverse range of malignant and benign conditions affecting women.[4;32] Although new technologies and techniques have been introduced that are replacing hysterectomy in some circumstances, it is still the most frequently performed major surgical procedure on women in the UK, North America, Australia and throughout Europe.[53;54]

Cervical cytology screening has been highly successful in reducing the incidence of cervical cancer in those countries that have adopted it. The UK has a national programme (NHSCSP) which is one of the most successful in the world; this is because it is free at the point of access, achieves full population coverage and has high uptake rates.[15;66]

However, use of vaginal vault cytology as a screening test in women following a total hysterectomy is only recommended for highly selected populations, as vaginal cancer is too rare to justify an organised screening programme.[24]

It has been suggested that some vaginal vault cytology testing is being undertaken inappropriately, particularly in primary care,[28] and so this study aimed to identify a cohort of women undergoing a hysterectomy and consider their entire screening history both before surgery and subsequently.[127] The aims of this study were established as:

- *Primary*: to describe the variation in hysterectomy rates and subsequent follow-up by use of the vaginal vault cytology test in the West Midlands region.
- *Secondary:* to inform the development of national guidelines by generating high-quality evidence about current practice with respect to vaginal vault cytology.

A pragmatic record linkage study was designed so that a cohort of women, having undergone a hysterectomy, could be identified from Hospital Episode Statistics. Then, their entire screening histories could be obtained from Open Exeter and merged with these data, supplementary data being obtained from individual histopathology laboratories where possible, using linkage techniques. Thus routinely collected, high quality, patient data could be utilised without the need for individual patient consent.

The database was to be anonymised as soon as practicable after linkage, and before any analysis occurred to minimise the potential for any harm to patients from this transient breach of confidentiality.

It transpired that HES and Exeter were rich sources of comprehensive, robust data. However, a combination of the PIAG stipulation that only NHS number could be used for linkage, inter-hospital variability and lack of reliable use of NHS number through the region, rendered the hospital data unsuitable for any more than very superficial description. The final study dataset was cleaned and validated and contained data on 6,141 women from the West Midlands region who underwent a hysterectomy operation, their entire cervical screening records prior to surgery and any cytology results in the four years after surgery.

The findings from this study are now summarised according to the original study objectives.

1. To estimate incidence rates for hysterectomy operations in the West Midlands region of the UK

The overall study demographics revealed an incidence of hysterectomy of 23 per 10,000 women per annum, and a median age of surgery of 48 years with a wide range of 17 to 94 years.

This incidence rate was lower than previous estimates[1] but is consistent with a reduction in the use of hysterectomy for the management of some benign conditions, and still makes it a very commonly undertaken operation. The average GP surgery of 6,000 patients will thus expect an average of seven women each year to have the operation.

2. To describe variations in incidence of hysterectomy and establish those factors associated with variability

The patient factors that were considered most likely to cause variability included age, deprivation, ethnicity and pre-existing medical problems including abnormal cervical screening and co-morbidities. External factors that were considered most likely to influence incidence were hospital and surgeon of treatment. Numbers were too small to investigate choice of surgeon and data was very limited on co-morbidities but the other factors were explored.

There was a very wide variation in hysterectomy incidence by age, with a peak incidence of 63 per 10,000 in the 45-49 years group, corresponding with the time of the menopause transition. This was not surprising and was consistent with previous research findings.[1] Age standardisation did not make any meaningful difference.

The study population was significantly more deprived (IMD) than the population of England with 27% of the study population in the most deprived quintile and 14% in the least deprived. However, deprivation scores were very similar to those for the West Midlands region,[158] which is itself somewhat more deprived than England overall. Age standardised incidence rates for hysterectomy varied significantly by deprivation score: those most deprived had an incidence rate of 25 per 10,000, compared with 20, per 10,000 in the least deprived quintile.

These findings suggest that women in more deprived areas may have greater morbidity or receive a different standard of gynaecological care than those from less deprived areas, which is compatible with previous studies.[12]

Ethnicity data, although only available for two thirds of the population, indicated that the study population had some differences from the background population of the West Midlands region. Black women (encompassing Caribbean, African and other Black groups) had an incidence was as high as 33 per 10,000. White women were the great majority and had an incidence of 23 per 10,000 (same as the overall population), in Chinese and mixed races numbers were too small to permit meaningful comment.

Ten women died during their hospital admission, five of whom had malignant disease. This represented 0.16% of the study population or a mortality rate of 1.6 per 1,000 hysterectomy operations, however when separated by underlying diagnosis the mortality rates became 7 per 1,000 for hysterectomy in cases of malignancy and 1 per 1,000 for benign indications, which is still higher than the quoted incidence.[9] This area requires further investigation.

3. *To describe cervical screening patterns prior to hysterectomy*

Preoperative cervical screening was undertaken on 5,787 women (94.23%) thus the great majority of the study population. Those women who were 'ever' tested underwent a median of five tests each, although this varied significantly by age. One in six of the whole cohort subsequently had some post operative cytology.

The result of the last cervical screening test before hysterectomy (the index test), was of interest with results suggesting cancer being more common in younger women and abnormal test results being more likely in women living in more deprived regions. Ethnicity was not associated with index test result although being of a nationality other than White British was associated with never having attended for cervical screening.

The index test was considered for use as a predictor of future diagnosis at surgery but, although obviously associated with operative findings, it is not sensitive or specific.

The application of a complex coding algorithm, from the WMQARC, to the study data, allowed entire screening histories to be classified and compared. The findings of this corroborated the data on deprivation and ethnicity even though the groups were created slightly differently from those using the raw study data.

4. To describe the current indications for hysterectomy in West Midlands

Malignant disease accounted for 11.6% of the study population, 3.0% for intraepithelial neoplasia but the great majority had surgery for benign indications (82.9%). Women frequently had several diagnoses documented but for the study purposes the 'worst' of these was used. CIN was noted more frequently in younger women.

Women with malignant disease were more likely to be white and were significantly older than the rest of the study population. Regression analysis of those factors associated with having a total or subtotal type of hysterectomy revealed significant associations with age and result of the index test, however these only accounted for a small proportion of the total and thus other factors may be more important, however, investigating these was beyond the scope of this study.

5. To establish the current pattern of follow-up after total hysterectomy by means of vaginal vault cytology test

Dividing the study participants according to hysterectomy type (using OPCS codes) allowed post operative cytology to be classified as vault cytology or continued cervical screening. Total hysterectomy was performed in 92.77%

The women who had total hysterectomies were considered further: vault cytology was undertaken on 9.35% of women who had benign disease, this was clearly inappropriate. Of women having a hysterectomy for carcinoma in situ or CIN, only 63% had any vault cytology, thus in the one group of women who are explicitly recommended to have some post operative testing, over a third did not have any.

Operative diagnosis was confirmed as the strongest predictor of having any vault cytology. Women who had vault cytology undertaken were more likely to be younger, less deprived and non-White than those who did not have vault testing. Having an abnormal index test result was clearly associated with having post operative cytology as was having a history of any abnormal cytology preoperatively.

Logistic regression analysis of 'patient factors' demonstrated that although age and deprivation score were associated with having vault cytology, the odds ratios were very small and the clinical usefulness of this observation is doubtful. Hospital of surgery was also a significant 'external' factor but overall impacted little on the fitted model.

6. To assess if vaginal vault cytology is being undertaken appropriately and establish those factors associated with inappropriate usage

Women having a hysterectomy for CIN were scrutinised: in addition to those not being tested at all (thus inappropriately not being tested), of those who were tested 24 only had one test (too little testing), 16 had two tests but over too great a time frame (too infrequent), 50 had more than two consecutive normal results (excessive testing) and just 13 (7.18%) were followed-up exactly in accordance with the national guidelines.[16] Thus, there was ample evidence of inappropriate over and under-use of vault cytology testing, even in the group of women that guidelines specifically single out for testing.

When those women having a hysterectomy for benign disease were considered closely, and the latest guidance applied, (including the suggestion that vault cytology be undertaken if a woman has less than 10 years of pre-hysterectomy cervical screening) the proportions having inappropriate testing increased, with inappropriate screening in 721 of 4,695 = 15.36% (407 tested completely inappropriately, 298 not tested who could have been, 16 correctly had one test but then had further testing with normal results).[89]

Regression analysis of those factors associated with inappropriate usage of vault cytology only identified index test result as being clinically important although age and deprivation score were related.

7. To describe the results of vaginal vault cytology with respect to histology at hysterectomy and establish those factors associated with having an abnormal result

With only 21 definitely abnormal vault test results (2.93%) in 717 women it was not possible to draw firm conclusions concerning factors predictive of abnormal vault cytology and regression analysis could not be undertaken. The only factor clearly associated with an abnormal vault result was diagnosis at hysterectomy, with CIN or cancer being related to subsequent abnormal vault cytology.

8. Additional findings of interest, supplementary to the original study aims

HES and Open Exeter Linkage: This study confirmed that linkage can be reliably undertaken even if just NHS number is available to the researcher, as a high ratio of perfect matching will be found. Thus future projects may seek to just use this identifier to minimise breach of patient confidentiality, reduce beurocracy and limit costs. Further research concerning data linkage studies would be facilitated by streamlining of ethical approvals processes, researchers contemplating similar research should be mindful of the many permissions required to obtain confidential data without explicit patient consent.

Hospital pathology laboratory data: This was a rich source of information but was difficult to translate between institutions, caution is recommended to researchers contemplating projects that may necessitate merging of data from a variety of hospitals that do not have similar software and coding standards. In future this problem should be overcome by improvements and standards of NHS IT systems. Further research is recommended but with the caveat that more patient identifiers can be used for validation.

West Midlands QARC Screening history algorithm: This novel, bespoke software has the potential to standardise summarising entire cervical screening histories and has potential to be developed for other applications. With only minor modification it was successfully used to code entire screening histories prior to hysterectomy and as such will allow for future collaborative research.

Inter-hospital variation: This accounted for some of the poor ethnicity data with a few hospitals clearly using invalid coding whereas others had up to 98% of women's ethnicity recorded. This is an area that should be improved in future as accurate ethnicity recoding in NHS records has become a higher priority recently.

Operation type: This was established for all but eight of the participants; sub-total surgery was more common than had been anticipated and this was particularly noticeable in younger women and women of non-White ethnicity. The reasons for this increase are not clear and warrant further study.

Death rate: During their hospital admission ten women died; a mortality rate of 16 per 10,000 hysterectomy operations or one per 625 cases. However, when split by diagnosis, five deaths were in women having a benign disease giving a mortality of five in 5,090 or one per 1,000, this is significantly worse than RCOG published risks of hysterectomy at one death in 4,000 operations. For malignant disease it was five in 713, or seven per thousand. There were no deaths in cases of CIN but numbers were small. These findings warrant further investigation as a matter of urgency.

Duration of post operative stay: With a median of five and mode of four days, this was unremarkable. However, data suggesting that 1.7% of women were sent home on the same day as major surgery requires further investigation. This may represent miscoding or the fact that women were actually transferred to another hospital to recuperate (although this was not documented appropriately).

If some women are being discharged home quickly this has implications for practice and if demonstrated to be a safe option (with the appropriate clinical safeguards), this has the potential for increased throughput of patients.

Overview of results

Data linkage of confidential routinely collected data is possible but requires multiple ethical approvals. Analysis of the study dataset confirms that hysterectomy is still commonly performed for a wide range of indications in the West Midlands. Ethnicity and deprivation of the patient have some associations with incidence of surgery (higher incidence in Black women and women who are more deprived).

Mortality appears to be worse than the currently quoted risks from surgery, at one death in 1,000 operations; this finding requires further validation and it is important that patient information and pre-operative consent should be amended to incorporate this figure if found to be accurate.

Results from a woman's preoperative screening history are associated with her likelihood of having subsequent post-operative vault cytology testing. Typically women had a median of five cervical screening tests prior to hysterectomy.

It has been confirmed that vault cytology testing is being undertaken inappropriately in a significant proportion of cases and national guidelines are not being followed closely.

For women with benign indications for surgery, over-testing was a concern, for those having CIN then testing too infrequently or not at all was the issue. For women who had malignancy at the time of hysterectomy there was significant variation in the numbers who were followed up by vault cytology suggesting that there is no consensus amongst gynaecologists about the role of this test.

Less than 3% of all women who underwent vault cytology ever had any abnormal results. Thus the test is only detecting abnormality in a small proportion of women which reinforces concern about its usefulness or appropriateness of application.

8.2 CONCLUDING OBSERVATIONS

Cervical screening

Use of WMQARC algorithm for the classification of entire screening histories should become the gold standard for future research and audit in this field. This will allow for valid comparisons between populations and make interpretation of study findings more generalisable.

The high quality data contained in the Open Exeter system is a rich resource for research and, if it can be made more accessible by improvements to the software or transferring the data to a more 'user-friendly' format, then the usefulness outputs could be increased significantly.

The UK cervical screening programme is a 'jewel in the crown' of the NHS and is an excellent demonstration of the positive impact that a well organised and funded screening programme may have. However, success in one programme does not guarantee success in all areas and any potential screening test must fulfil many established criteria before it should be used.

Use of vaginal vault cytology is currently outside the remit of NHSCSP; however, by suggesting a place for its use in its published guidelines, the NHSCSP has taken on responsibility for providing the highest standard of evidence based guidance to healthcare professionals. There is clear evidence that these guidelines, like many others, are not being adhered to, this may be due, in part, to their complexity.

Hysterectomy

Hysterectomy has been demonstrated to be declining in popularity. This is likely to reflect the introduction of minimally invasive surgical techniques, less destructive endovascular treatments and an increase in pharmacological treatment options over the past three decades.

Notwithstanding, the average GP surgery still has seven cases per annum (23/10,000 women pa) and in areas with of high density of women of Black ethnicity or a higher than usual proportion of peri-menopausal women, this incidence may be substantially greater.

The death rate in women having hysterectomy is not insignificant: 1 per 1,000 women having the operation for benign indications and 7 per 1,000 for those with malignancy. These are higher than the quoted RCOG figures[9] and this finding requires closer inspection as a matter of urgency so that in future women are realistically informed, prior to surgery, of the potential risks involved. The presence of disseminated malignancy and significant co-morbidity obviously increase the risks of any surgery and if these women were excluded from this study then the mortality rates would be closer to the quoted figures, but still show a four-fold increase.

Subtotal hysterectomy seems to be increasing in popularity in UK, a somewhat odd finding which does not have a good scientific backing.

Thus, this area requires further investigation to establish the reasons behind this observation: are certain hospitals or individual specialists expressing their preference or is this a reflection of increased patient choice? If this is a reflection of patient preference, then are women making a fully informed choice or is there a media driven effect? Is it because patients are becoming increasingly obese and thus surgery is technically more challenging? This topic should ideally be explored using qualitative methodologies; possibly starting with a questionnaire survey of women who had recently underwent a hysterectomy, then purposively interviewing those who had researched the subject or made a conscious decision to have a certain variant of the operation.

Vault cytology

This study has confirmed that vault cytology tests have a low rate of detection of abnormalities and makes a poor screening test as vaginal cancer is very rare. Cytological testing of the vaginal vault was never intended by Papanicolaou, when he developed his technique for examining a scraping of endothelial cells from the transformation zone of the cervix.[73] More recently, the introduction of liquid based cytology techniques for analysing samples has exacerbated the situation as modern 'soft brush' sampling devices are even less useful to obtain samples from the ill defined vaginal vault than the 'extended tip' Aylesbury spatula.

The study has confirmed that the national guidelines concerning vault cytology are not being closely adhered to by clinicians, even in women who may benefit from some form of follow-up.

For women with a malignant diagnosis, opinion amongst gynaecologists is obviously divided as less than 20% of this population receive cytological follow-up. If the test was felt by specialists to be of use then a significantly larger proportion of these women would have been expected to have undergone testing.

To definitively answer the question of the value of vaginal vault cytology would require a very large prospective cohort study of women followed up for decades. This is unlikely to ever be possible in view of the extremely high cost of such studies and the limited potential benefit. Thus, this study as a pragmatic alternative should be used to guide policy makers in the future.

Further cost effective research, building on these findings, could include several areas: it would be helpful to know what gynaecologists and primary healthcare professionals think is appropriate and would like to see happening with respect to follow-up after hysterectomy. This could be achieved with a combination of questionnaire surveys and interviews.

In this climate of valuing patient choice, it is surprising that the literature does not address the issue of whether or not patients would value post operative testing. Thus, the viewpoint of patients having hysterectomy, for a variety of conditions, concerning their subsequent follow-up, should be sought.

Given that vaginal vault cytology: is being used inappropriately (both over and under use) suggesting confusion by clinicians; has low rates of disease detection; sampling methods are no longer routinely taught to primary care clinicians at training updates and liquid based cytology techniques are not designed to facilitate adequate sample collection. It is recommended that vaginal vault cytology should no longer be routinely undertaken in primary care.

Instead, it is time for specialists responsible for undertaking hysterectomy operations to acknowledge the limitations of the test and to retain clinical responsibility for any ongoing surveillance. Thus, the clinician undertaking or supervising the original operation will have a full picture of the individual patient and their risks and can weigh-up all these factors. Additionally, if follow-up is undertaken via colposcopy services then the vaginal vault can be examined closely by the colposcope and stained to identify high risk areas for more accurate sampling or biopsy.

It would be helpful, to all responsible for undertaking cervical and vault cytology testing in both primary and secondary care, if the national guidelines were to be revised and amended to take account of this research and the suggestions herein.

Thus, unnecessary testing could be minimised with consequent savings to women and the NHS: psychological, physical and economic. Additionally, those women who may genuinely benefit from ongoing vaginal vault cytological surveillance will receive more appropriate clinical care.

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APPENDICES

Appendix A. A systematic review of vault cytology – full published paper

Vaginal vault smears after hysterectomy for reasons other than malignancy: a systematic review of the literature

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ABSTRACT

Background: Vaginal vault smears are used to detect persisting neoplasia of the lower genital tract after hysterectomy. Recent data suggest both widespread use and uncertain evidence of their effectiveness.

Objectives: To identify and synthesise evidence on the use and effectiveness of vaginal vault smears and to assess the quality.

Search Strategy: 'vault smear' OR 'vaginal vault smear' OR 'cervical vault smear' OR ('Hysterectomy') AND ('Follow up' OR 'Smear').

Selection Criteria: Primary research, women who had a hysterectomy and were followed up by vault cytology.

Data Collection and Analysis: Systematic search (8 electronic databases), supplemented by contact with experts and review of bibliographies. Two independent reviewers determined eligibility/validity and extracted data concerning test performance characteristics. Quality was assessed according to established criteria.

Results: 441 unique references, only 19 suitable. Quality of studies varied considerably and few were of 'high' methodological quality. Studies were geographically diverse and published over 40-years in 16 journals. From the higher

scoring papers there were 11 656 hysterectomies (6 546=benign, 76=CINI/CINII, 5 037=CINIII). Proportions of abnormal vault smears and abnormal biopsies during follow-up increased with worsening histology at hysterectomy ($p<0.0001$ and $p=0.0001$). There was only one report of vaginal cancer subsequent to hysterectomy for CIN and insufficient data to allow for reliable meta-analysis.

Conclusions: Vault smears cause anxiety, consume resources and their value is largely unproven. Inconsistency of study design and limited methodological quality means that the value of vault smears could not be established. High quality research is required to ensure that guidelines are evidence based.

Key Words: Systematic Review; Vaginal vault smear

INTRODUCTION

It has been suggested that too many vaginal vault smears are being undertaken both in the USA[1] and the United Kingdom.[2] The value of this test, in the follow-up of women after hysterectomy, has not been established and guidelines are based upon consensus opinion.

By the age of 65 the proportion of women having a hysterectomy reaches a third in the USA[3] and 20% in the UK (60 000 procedures annually).[4] Subtotal surgery (sparing the cervix) is undertaken in less than 3% of the hysterectomies performed in the UK.[5] Total hysterectomy includes removal of the cervix-uteri leaving the vagina as a blind ending pouch; since the cervix has been removed there is no possibility of the development of a primary cervical cancer and thus no indication for routine cervical screening. Papanicolaou (Pap) smear tests[6] of the vaginal vault are a means of detecting recurrent invasive or pre-invasive disease of the lower female genital tract in women who do not have a cervix-uteri.[7]

Benign indications (e.g. excessive bleeding or fibroid disease) account for over 90% of hysterectomies in the UK.[5] The proportion of hysterectomies performed for cancer or pre-cancerous lesions has been reported to range from 6-10%.[8] After surgery, current policy in the UK is to follow-up with vaginal vault smears those women who have had a hysterectomy for high-grade pre-invasive disease of the cervix.[9] However, recent work suggests that practice varies amongst clinicians and many additional women may receive follow-up smears.[2]

The purpose of undertaking vault smears on asymptomatic women who had no abnormal cervical pathology at hysterectomy is to screen for vaginal intraepithelial neoplasia (VAIN) and prevent vaginal cancer. However, VAIN is 150 times less common than cervical intraepithelial neoplasia (CIN) and vaginal cancer is one of the rarest gynaecological malignancies (0.7 per 100 000 women in UK).[10] Recognised risk factors for VAIN include: CIN, immunosupression, genital warts / human papilloma virus (HPV) infection, radiation therapy and smoking.[10] Besides VAIN, the only group of women appearing to be at increased risk of primary vaginal cancer are those whose mothers took diethylstilbestrol during pregnancy.[11]

Opinion regarding the role of the vault smear has changed over time: In the 1950s there was enthusiasm for follow-up after hysterectomies demonstrating the presence of carcinoma-in-situ.[12,13] Since the 1990s, this strategy has been questioned, and it has been suggested that too many vault smears may be being undertaken.[1,3] In 2001, it was estimated that approximately 11 million vault smears per annum were being performed 'unnecessarily', out the 12.5 million women who had a hysterectomy and were continuing to have Pap smears[1], in the USA, the study concluded that only 7-15% of women should require vault smears after hysterectomy (or cervical smears after sub-total/supracervical hysterectomy). If more than 80% of vault smears are unnecessary, this represents a huge waste of resources and may be the cause of unwarranted anxiety and inconvenience for women.[14]

In 1996 Pearce et al[15] reported the results of screening a large cohort of women who had previously undergone hysterectomy for benign indications. The positive predictive value of the vault smear, as a means of screening women who have undergone hysterectomy for benign reasons is low[16] and 10 years ago it was recommended that "the use of the Pap smear after hysterectomy, for benign disease, should become a thing of the past".[17]

This study aimed to establish the evidence base for the use of vaginal vault smears subsequent to hysterectomy for benign or pre-cancerous conditions.

METHODS

This systematic review[16] aimed to identify all studies that either evaluated the vault smear test, or which reported the follow-up of a series of patients treated by hysterectomy for reasons other than malignancy, and contained data to enable the value of vault smears to be estimated.

Searches were performed on the following electronic databases: Medline (from 1966), Embase (from 1980), CINHAL (from 1982), CancerLit (from 1960) NHS Centre for Reviews and Dissemination, Database of Abstracts of Reviews of Effectiveness (NHSCRD – DARE), Turning Research into Practice (TRIP: from 1986), Cochrane Collaboration Database, and Web of Science (WOS). The search terms comprised 'vault smear' OR 'vaginal vault smear' OR 'cervical vault smear' OR ('Hysterectomy' AND ('Follow up' OR 'Smear'). The specific search strategies (i.e. text words or index terms) were varied according to the search engine

(Appendix A). Citations were downloaded into Reference Manager to facilitate identification of duplicate entries and for ease of handling. Electronic searching was supplemented by asking authors of papers relevant to the subject of this review to assist with the identification papers that pre-dated electronic search facilities, or of relevant unpublished data.

Two authors independently scanned the titles and, where available, the abstracts of all articles identified by the electronic searches, excluding those that had no relevance. Complete copies of all remaining references and those where a decision could not be made on the basis of the title or abstract alone, were requested and two authors independently reviewed these to identify all eligible publications. Any disagreements were resolved by discussion with a third reviewer.

Papers were 'eligible' for inclusion if they reported on a population of women who had undergone a hysterectomy and at least some of the population had vault smear tests. Case reports or expert opinion were excluded. Where the study population comprised a cohort of women with abnormal smears and where the number of women having had a hysterectomy was not stated (i.e. the rate of abnormal smears subsequent to hysterectomy could not be established) the publication was also excluded. All papers selected as eligible for inclusion had their bibliographies reviewed to identify any further papers of relevance to the review. Eligible papers were considered in full by two independent reviewers using a standardised pro-forma (Appendix B) to determine the relevance of the papers to the aims of this

review. Two reviewers undertook independent data abstraction, any discrepancies in data abstraction were discussed and consensus reached.

Included papers were scored, by two independent reviewers, for methodological quality. The scoring system was modified from the validated NHS Critical Appraisal Skills Programme (CASP) tool for assessing a diagnostic test[18] (Appendix C). Again, any disagreement between the reviewers was resolved by consensus. The Quality Score (QS)[19] was made up of points being awarded for a "Yes" response to different aspects of the methodology, resulting in a possible score of between zero and 10 for each. Papers having a QS greater than six were deemed to be of a 'good' methodological quality, however, even validated quality scoring systems can be criticised[20] so the data from poorer quality papers was retained for comparison and three reviewers considered the methodological aspects of all studies at length.

RESULTS

The Literature Searches

The systematic review identified 526 citations in total, 453 from electronic databases, seven from experts in the field and 66 from the bibliographies of included papers. There were 441 unique references once duplicates were excluded (371 from electronic sources, four from experts, 66 from bibliographies). Of these 319 were excluded on the basis of title and abstract alone; a further 102 were excluded at eligibility assessment. Thus, 20 research publications were eligible for inclusion. Of these, two reported the same piece of research and were published by

the same group in the same year;[21,22] the more comprehensive was included.[22] This gave a total of 19 studies:13 from electronic searches, one from experts and five from bibliographies. Table 1 summarises the source of publications.

All identified studies utilised a form of cohort design and one had a control group[23]. The included papers were published between 1963 and 2000 in 16 different journals, with 11 published prior to 1990 (58%), (Table 2).

Three of the papers contained information about women who had more than one histological diagnosis.[23-25] Five papers followed up women after hysterectomy for benign disease.[15,23,26-28] There were no papers concentrating exclusively on women who had CIN I or CIN II, the majority of papers considered follow up after carcinoma-in-situ or CIN III.[22,24,29-39]

Data Extraction

Table 2 summarizes the abstracted data from all 19 included papers. Cytological nomenclature has changed over time and reports from early studies have been 'translated' into the currently accepted terminology to allow for comparison.[40,41] The authors' conclusions about the study, if related to the role of the vaginal vault smear, are reported along with our comments on the significance of the results. Quality scores (QS) ranged from 3.5 to 9 indicating wide variability in the methodological quality of the publications; only nine received a QS of ≥6.

The 19 studies were geographically diverse with six from North America, five from the UK, five from mainland Europe and two from New Zealand. One was a prospective cohort study, the rest were retrospective, and they were published in 16 different journals. For each paper the number of women having a hysterectomy and the number subsequently followed up by means of a vault smear (N) is given (range 4 to 5 682). All available outcomes data were abstracted including: (1) number of abnormal vault smears, (2) number of abnormal vaginal vault biopsies (i.e. histological confirmation of the presence of VAIN or other pre-malignant change but not frank malignancy), (3) number of vaginal cancers identified subsequent to hysterectomy. Tables 3i-iii summarise the numbers of 'events' documented in only the papers of better methodological quality (QS≥6).

Narrative review

The papers considered women with a variety of diagnoses at surgery, ranging from benign through to micro-invasive cancer, although the majority considered women with cervical intraepithelial neoplasia (CIN). The papers were divided into two main categories, women who had benign disease at hysterectomy and those who had CIN; these mainly comprised CINIII, a smaller number of papers also included cases of CIN I and II.

Follow up after hysterectomy for benign histology: Five studies were identified of which three were of better methodological quality. [15,26,28] Only one provided data suitable for life table analysis, this was a retrospective case note review and included women who had abnormal cytology before surgery but a benign diagnosis

at the time of surgery.[28] All concluded that there is little benefit in follow up by vault smear screening: “The target condition is not common. . . less screening may be more desirable”,[26] “there are currently no known scientific benefits from routine screening. . .and there can be possible risks”,[28] “because of the low prevalence. . .and poor positive predictive value of the test routine screening. . .is probably not necessary”.[15]

Follow up after hysterectomy for CIN III: This diverse group of 15 papers only included six of better methodological quality.[22,24,29,30,32,38] Three papers included cases of CIN I and CIN II, in addition to CIN III,[24,25,32] one paper also included benign cases but comprised a population of women who were HIV positive – a population not comparable to the general population and therefore excluded from further analysis.[23]

The six best quality papers were published over a 40 year span and their recommendations changed over time; in the earliest paper the conclusion was “of the utmost importance is thorough and long-term follow up”, whilst the most recent stated “The highest incidence of VAIN is found in the first two years after hysterectomy, after that incidence falls to that of the general pre-hysterectomy population.”[32]

Analysis

Outcomes after hysterectomy:

- Subsequent to benign indications (n=6543), 1.8%(117) of women had an abnormal smear, 0.12%(8) had an abnormal biopsy and no cancers were identified.
- Subsequent to CIN I or II: 3.1% had an abnormal vault smear, 1.3% an abnormal biopsy and no cancers were detected.
- Subsequent to CIN III, 14.1% of women had an abnormal smear, 1.7% an abnormal biopsy and one vaginal cancer (0.03%) was detected. This was the only report of invasive vaginal cancer, subsequent to hysterectomy for CIN III.

Abnormal subsequent events (i.e. abnormal smear (χ^2=522.6, 2df, p<0.0001) and abnormal biopsy (χ^2=86.1, 2df, p=0.0001)) were positively associated with the histology at hysterectomy (benign, CINI/II, CINIII) i.e. more adverse outcomes with increased severity of disease.

Follow up after hysterectomy for benign histology: Table 4i contains details of all studies reporting follow-up after hysterectomy for benign reasons with follow up information irrespective of methodological quality. Only one paper,[26] (QS=6) included sufficient censoring and event data to enable estimation of a survival distribution.

Follow up after CIN III: Events occurring during follow up after hysterectomy for CIN III are summarised in Table 4ii which includes all papers from the review, irrespective of QS.

DISCUSSION

Summary of the evidence:

Vaginal cancer is very rare. This project aggregated data from studies following-up over 6800 women after hysterectomy for benign indications, CIN I and CIN II; despite up to 50 years follow-up, no cases of subsequent vaginal cancer were identified. Only one case of vaginal cancer was observed, three years after hysterectomy, in the cohort of 3 569 women having hysterectomy with reported evidence of CIN III. Unfortunately, all the studies following up women after hysterectomy with CIN III had significant methodological or reporting flaws. These results are compatible with the very low background incidence of primary vaginal cancer (approximately 7 per million women per annum).[42]

There is little good quality evidence concerning the role of vaginal vault smears and there are insufficient data to enable the calculation of robust aggregated assessments of the sensitivity or specificity of the test. Most of the observed events occurred within the first two years of follow-up; 46 of the 48 documented abnormal vault smears occurred within five years of hysterectomy.

Of the six best quality studies, two considered data from women who had a hysterectomy for benign indications or CIN I/II and four studies considered women who had CIN III. The authors' conclusions following hysterectomy for benign conditions were largely opposed to the use of the vault smear test for screening whereas recommendations following CIN III ranged from advising annual smears to

a more intensive regimen for two years followed by reversion to routine smears with the frequency recommended by the national screening programme (Table 2).

Justification

UK guidelines[9] recommend that vault smears should only be undertaken where there is reasonable suspicion that their pre-existing cervical pathology has not been fully treated (i.e. For women on routine recall for at least 10 years prior to hysterectomy and no CIN in the sample at hysterectomy, no vault cytology is required; For women with less than 10 years routine recall and no CIN at hysterectomy, a sample should be taken 6 months after surgery and there should be no further cytology if it is negative; For women with completely excised CIN , a sample should be taken from the vault at 6 and 18 months after surgery, there should be no further cytological follow-up if both are negative). These guidelines are not based on gold standard evidence: they were derived from expert opinion. Thus, there is a need for good quality research to establish the evidence for continued surveillance and re-assess the appropriateness of current guidelines. This systematic review has aimed to address this need.

Methods

Pooled estimates of sensitivity and specificity for the vault smear test for each histological subgroup were anticipated outcomes of this review, but the variability in reference populations, incompleteness of data on censoring or confounding and large losses to follow up meant the data were insufficient for meta-analysis.

Searches of electronic databases and bibliographies of included papers provided the richest source of papers for inclusion, Medline provided almost half of the identified papers with bibliographies providing studies pre-dating electronic search engines and they were published in 16 different journals. The total number of women followed up by vault smears in all the studies was 13 338 (range 4–5 682; mean = 744; median = 220).

Quality Scores

Quality assessment scales for identifying trials of genuinely high quality are problematic[20], however this limitation was considered from the outset and all data retained for consideration. Three reviewers all agreed with the study 'quality' based on the modified CASP score and so no deviation from this was deemed necessary. The mean quality score was 5.5 (range 3.5–9, SD=2.02), with only 6 papers having a QS greater than six and thus being deemed of 'good' methodological quality. There was no correlation between year of publication of the study and the quality score for that study, (Spearman correlation coefficient=0.133, p=0.588). The low quality scores reflect the fact that these data have been abstracted predominantly from studies that were not designed to provide data in the format required for this type of review.

CONCLUSIONS and IMPLICATIONS

This comprehensive, systematic review has collated and assessed the available literature relating to the appropriateness of follow-up subsequent to hysterectomy for indications other than cancer. The better quality studies had a combined study

population of 11 656 hysterectomies of which 6 543 were for benign disease, 76 for CIN I/II and 5 037 for CIN III. Nevertheless, incompleteness of follow up and recording prohibited meta-analysis of these data and it was not, therefore, possible to provide robust estimates of the value of the vaginal vault smear test in the follow up of women who have had a hysterectomy for reasons other than malignancy.

Based on the available evidence the current UK guidelines[9] appear reasonable. However this study confirms the need for definitive research to determine the appropriate duration and frequency of vaginal vault smears after hysterectomy for reasons other than cancer. Women's views concerning the appropriateness of follow-up and a better understanding of the anxiety related to vault smears are also required if appropriate, acceptable and evidence-based guidelines are to be developed.

As it is not practical to undertake a prospective randomised controlled trial (because vaginal cancer is rare and such a trial would have considerable ethical implications), epidemiological techniques continue to offer the most practical approach to answering some of these questions. A large, prospective audit of a cohort of women undergoing hysterectomy for reasons other than cancer could establish the frequency and characteristics of those who later develop VAIN and/or vaginal cancer.

Any future decisions concerning the use of the vaginal vault smear must consider the potential harms of screening, including possible over-diagnosis (false positives)

and over-treatment, as well as the potential benefits. Women's views concerning the appropriateness and duration of follow-up need to be established. It is known that in cancer screening programmes, false positive results cause a high level of anxiety.[14]

This review has raised a number of important issues. Existing published research inadequately defines the clinical, financial and personal consequences of performing vault smears. The vaginal vault smear may be regarded as a 'low priority area' when compared with the large number of smears undertaken within cervical screening programmes. However, the public health services are required to justify all expenditure and further research in this subject is long overdue.

Finally, we conclude that there is currently as there is no evidence to suggest that there is any demonstrable benefit in screening after hysterectomy for benign disease and, therefore, there is no evidence to support changing current guidelines for screening after CIN I/II. Screening after a diagnosis of cancer is outside the scope of this review. Screening after CIN III to five years is proposed by some authors, however, the data from this review indicate that 95% (46 of 48) abnormal smears occurred within two years and only one case of vaginal cancer was identified in all of the reported series. The value of the vaginal vault smear test as a screening tool after hysterectomy for reasons other than cancer is not supported by the existing literature.

Data access and responsibility: Helen Stokes-Lampard had full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest statement for all authors: None

Authors' contributions: All authors have approved the final manuscript. SW, CW and SK conceived the study, HSL, SW, CW and SK developed the methodology. HSL and SW conducted the searches, HSL, SW and AR obtained the data, appraised it and undertook the literature review. RH, HSL, SW and AR undertook the analysis. HSL drafted the manuscript with all authors contributing to its critical revision. SW supervised HSL throughout this study.

Funding: Sue Wilson is funded by a UK, Department of Health National Primary Care Career Scientist Award, Helen Stokes-Lampard and Angela Ryan are funded by UK, Department of Health Researcher Development Awards. These funding sources had no other role in this study.

Acknowledgements: Charlotte Mann assisted with electronic searches, obtaining material and reviewing papers, Linda Grovesnor assisted with writing the paper.

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Tables

Table 1. Evaluation of references by source

Source of papers	Total no of references	No of unique references No (%)	Excluded Papers	Included references	Sensitivity of source	Precision of source
Medline	147	147 (33.3)	138	**9**	0.06	0.47
Cancerlit	64	41 (9.3)	39	**2**	0.05	0.11
EmBase	31	11 (2.5)	9	**2**	0.18	0.11
NHSCRD	117	117 (26.5)	117	**0**	0	0
Cochrane	44	35 (7.9)	35	**0**	0	0
Trip	48	18 (4.1)	18	**0**	0	0
Cinhal	2	2 (0.5)	2	**0**	0	0
WOS	2	0 (0.0)	0	**0**	0	0
Bibliographies	66	66 (15.0)	61	**5**	0.08	0.26
Experts	7	4 (0.9)	3	**1**	0.25	0.05
TOTALS	**526**	**441**	**422**	**19**	**-**	**1.0**

Table 2. Results table summarizing all papers finally included in the review

Study **Author,** Region Method, Year Reference	**Study Population** **Number of women**	**Inclusion details**	**Results and Authors conclusions** **n1** = numbers of abnormal vault cytology tests* **n2** = numbers of biopsy proven vaginal dysplasia **n3** = numbers of invasive cancers	**Reviewers Comments** **Quality Score QS = (0-10)** (score>6 = 'good' quality)
Berget County of Maribo, Denmark Prospective population cohort study 1972	243 had a hysterectomy subsequent to a cervical abnormality: 8 = Slight / Moderate atypia 206 = CIS 29 = Stage IA **N = 237** had vault smears	Followed up from 2-30 months by vault smear plus clinical examination & questionnaire. Excludes 13 cases of pre-existing invasive disease	237 followed up from 2-30 months by vault smear plus clinical examination & questionnaire **n1 = 3**: 4 actual abnormal smears but 1 awaiting data so excluded. **n2 = 3**: Carcinoma in situ 2/206 Stage 1a 1/29 16/237 women regretted hysterectomy. Therapeutic conization may be more appropriate for young women with stage 0.	*Follow up was short term only thus limiting usefulness of data.* *Incomplete information regarding proportion of patient followed-up. Possible that study underestimates true event rate.* QS = 7.5
Boyes British Columbia, Canada Cohort study 1970	Population offered free cytology service **N=2849** had vault smears **N = 159** followed up after micro-invasive disease detected	70% of population had at least one smear during study period: 1-5yrs = 1837 6-15yrs = 993 >16yrs = 19	**n2 = 24**: 12 = recurrent, 12 = new cases 3/24 = invasive ca, 19/24 = vaginal CIS 2/24 = occult invasive disease 14 within 5yrs, 22 within 10yrs, All within 15 yrs. **n2 = 4**: detected 1-5 years, **n3 = 1**: detected at 20months Hysterectomy does not mean the end of follow-up as there is a significant risk of the development of subsequent disease in the vaginal vault. Patients require careful & prolonged cytological follow-up for the rest of their lives.	*An unknown number had a hysterectomy. Large cohort study. No definition of how recurrent or new disease is distinguished.* *Authors' conclusions were influenced by higher rates of subsequent disease observed in sub-groups with micro-invasion and occult disease.* QS = 8
Fawdry UK, SE Scotland Retrospective Cohort from cytology records 1984	1062 women had hysterectomies for confirmed carcinoma in-situ or severe dysplasia **N = 810** had vault smears	1035 = CIS 27 = severe dysplasia Follow up: 253 regular vault smears, 557 had some vault smears	**n1 = 64:** but 62 were only 'grade 2 smears', 1 = unknown, 1 = presented symptomatically. **n2 = 12**: Presented at: 8months (1), < 12months (8), 1-2years (2) **n3 = 1** With improved management it is hoped that early 'recurrences' will be come less evident. However, at least 2 smears in the 2years after hysterectomy seem essential. Subsequently, for most, the very low detection rate does not justify an annual hospital visit with its attendant anxieties.	*Comprehensive study, focusing on the follow-up of CIS.* *Losses to follow-up may underestimate the true event rate.* QS = 7.5
Gemmell UK, Tayside region of Scotland	341 had a hysterectomy for CIN III	All asked to attend for regular vault smears for at least 10 years	**n1 = 9** **n2 = 3:** at 9 & 46 months and 16 years. Incidence of VAIN following hysterectomy for CIN III	*Well-designed study with sufficient follow up. Losses to follow-up have been excluded from the denominator and may result in an over-estimate of the incidence of disease.* QS = 9

Retrospective review (Cohort) 1990	**N = 219** had vault smears		was 0.91%...75% of abnormal vault smears reverted to normal without any active intervention... Little evidence to justify screening women who have undergone hysterectomy for CIN III any more frequently than the general population. Follow-up of women after hysterectomy for CIN III should involve 6-monthly smears for the first year with a third smear at 2years. If these smears are normal the woman could revert to the national screening programme.	
Halberg Denmark Cohort, (unclear if retrospective or prospective) 1969	10,200 women undergoing a examination **N = 49** had a hysterectomy for carcinoma in situ and were followed up by vault cytology		**n1 = 4** : 'atypical cells' at 2; 5; 5; 6yrs **n3 = 1:** invasive carcinoma with metastases at 18months post hysterectomy Need improved measures of diagnosis.	*Study population, duration & frequency of follow up incompletely described. Outcome of patients with atypia not documented.* QS = 5
Hellberg Sweden, Retrospective review of records 1987	90,000 fertile women served by a Swedish hospital **N = 154** Had CINII or worse at hysterectomy and had vault smears	Followed up with colposcopy and cytology twice a year for 2 years then annually Average duration of follow up = 10.3 years	**n2 = 4**: 2 'within 1 year', 2 at 1-2 years 1 = CINI, 2 = CINII, 1 = CINIII. **n3 = 0** The cure rate for hysterectomy is 99% (152/154). The results of conization are comparable to those for hysterectomy. Disease may recur after as long as 15-20 years, and patients therefore need to be regularly followed up, probably a minimum of 10yrs.	*Study aimed to compare outcomes from conization, cryosurgery and hysterectomy. Outcomes by initial histological diagnosis and completeness of follow-up not documented for sub-group treated by hysterectomy. Conclusions relate more to follow up after conization or destructive treatments of CIN, rather than after hysterectomy- data does not support the authors' conclusions.* QS = 3.5
Kalogirou Greece Cohort study 1997	993 women undergoing hysterectomy for CIN III. **N = 793** had vault smears	All had CIN and completed 10 years follow up: 6monthly for first year, annually thereafter	**n1 = 210** **n2 = 41:** VAIN Mean age at developing VAIN = 57 (35-75yrs) <1yr since hysterectomy = 6, 1-2years = 12, 2-5yrs = 20, >5yrs = 3 (up to 10yrs) Stage at detection: VAIN I = 4, VAIN II = 10, VAIN III = 27. In 21 (51%) cases the grade corresponded to original cervical lesion Incidence of VAIN in women who had completed 10yrs follow up was 5.1%. Vault cytology provides a suitable and acceptable test for detection . . . and is therefore indicated in follow up after hysterectomy for CIN. Cost must be justified in terms of benefit . . . (vault smears) still cause considerable stress and anxiety to women. . .smears should be performed every six months for the first two years then annually to five years. Follow up should include colposcopic review on each examination. . . The	*Appropriately designed study with good follow-up. Limited information about characteristics of population.* *Lack of clarity as to whether entire study population was CIN III.* QS = 7.5

			highest incidence of VAIN is found in the first two years after hysterectomy, after two years the incidence similar to that of general pre-hysterectomy population - 0.7/1000. Patients with at history of CIN before hysterectomy represent a higher risk group.	
Kirkup UK, Sheffield Retrospective cohort 1979	**N = 112** women had hysterectomy for CINIII and all were followed up with vault smears	Followed up for a minimum of four years and where the first two post-operative smears were normal	**n1 = 0** Recurrence of new lesions no higher than that in the general population . . . residual CIN after treatment should be detected by the first 2 post-operative smears. New lesions of CIN may occur but not more commonly than in the general populations and that the sudden occurrence of a possible 'second type' carcinoma. . . is rare.	*A highly selected population. Characteristics of population and number of excluded cases not provided.* QS = 5.5
Kurian UK, Edinburgh Retrospective cohort of computerised records 1999	**N = 34** had a hysterectomy for glandular neoplasia of cervix and were followed up by cytology	Women identified from pathology dept files, with glandular dysplasia, in-situ and invasive disease and treated by hysterectomy	**n1 and n2 =** unknown. No recurrent abnormal glandular cells on follow-up for patients with LCGIN or micro invasive disease. CGIN is a precursor of invasive adenocarcinoma. Important to ensure adequate free margins for patients with glandular precursor lesions not treated by hysterectomy.	*Study included 80 cases treated by diathermy loop excision. Unable to disentangle those women who had a hysterectomy from the rest of the cohort. Time to identification of CIN not stated.* QS = 5
Liukko Finland, Turku Retrospective cohort, review of case-notes 1978	245 women with CIS treated at a University Hospital. **N = 160** had vault smears	Followed up for 5 to 10 years	**n2 = 9:** 2 dysplasia, 4 CIS, 3 invasive on biopsy. Recurrences all occurred between 3months - 4yrs Recurrence may also be a new epithelial lesion on the basis of a multi-focal mechanism of production. Cytologic and colposcopic follow up of these patients is thus necessary.	*Lack of clarity concerning subset of study population who were treated by hysterectomy.* QS = 3.5
McIndoe New Zealand, Aukland Retrospective cohort, case-notes review 1969	539 women with cervical CIS. **N = 175** had vault smears	Followed up 1-17yrs (6.5 mean)	**n1 = 9** **n2 = 4:** at 0,6,7,7years Our conservative attitude to diagnosis and treatment of CIS is reinforced by the rarity of invasive vaginal cancer in these cases. No more . . .than periodic clinical, cytological and colposcopic examination is necessary.	*There is a lack of clarity with respect to study population and timing of abnormal smear results.* QS = 3.5
McIndoe New Zealand, Aukland Retrospective cohort, case-notes review 1984	**N = 250** women with CIS had a hysterectomy and all were followed up with vault smears	Follow up for 5-28 years at 3, 6 months & then annually	**n1 = 33** at 2 years (13.2%) **n3 = 8** cases of invasive disease, 1 at 1year, 2 at 1-5 years, 1 at 5-10 years and 4 at over 10 years. CIS cervix has significant invasive potential. Importance of observing patients for a long period is apparent. Patients with continuing abnormal cytology . . . are 24.8 times more likely to develop invasive carcinoma.	*Watch and wait policy and lack of intervention when abnormal smears occurred may have led to a higher than expected rate of invasive disease. Same series as 1969 paper.* QS = 5.5
Michalkiewicz Poznan, Poland Retrospective cohort, case-	701 Women with epithelia dysplasia **N = 172** had vault	Follow up 3monthly for 3years then 6monthly to 5yrs.	**n2 = 2** recurrences 2/160 = 1.25% after carcinoma in situ (11 & 22 months). The most frequent cause of recurrence seemed to	*Not possible to determine grade of dysplasia*. QS = 6

notes review 1963	smears	Dysplasia = 12, Carcinoma in situ = 160	be insufficiently radical treatment . . . The rarity of recurrence does not contraindicate conservative methods of treatment . . . Of the utmost importance is thorough and long-term follow-up.	
Miller USA Retrospective cohort, review of records 1987	3008 black women seen in a cancer-screening clinic **N = 775** hysterectomy for 'benign' reasons and had vault smears	Followed up by vault smears annually. Time from hysterectomy ranged from 1yr to >30yrs, 78% >5yrs previously	**n2 = 1**: vaginal dysplasia. (0.13%) **n3 = 0** The absence of carcinoma in the post-hysterectomy group suggests that although an annual physical examination is indicated, the time interval between performances of the Pap test may be lengthened. If one asymptomatic cancer had been detected, the $10,000 cost would have been justified.	*Incomplete information on follow-up. Possible that all subsequent cases not traced or included.* QS = 5
Pearce New Orleans, USA Retrospective cohort 1996	6265 women who had vaginal smears at a large inner-city charity hospital. **N = 5,682** had a hysterectomy for 'benign disease' and had vault smears. 99% = low socio-economic class	83% Black, 9% White, 5% Hispanic, 3% other race. The number of women with benign indications for hysterectomy was estimated from a sample of 150 cases	**n1 = 79** **n2 = 5** **n3 = 0** Positive predictive value of pap smear for detecting vaginal cancer – 0%. For detecting VAIN 6.3% On average, 19yrs from hysterectomy to first abnormal smear. Because of the low prevalence of disease and poor PPV of the test, periodic, routine screening by vaginal Pap smears is probably not necessary for women who had hysterectomy for benign disease. Vault smears should be considered only for women with a history of cancer of the genital tract or CIN III because they have increased risk of disease.	*Hysterectomy number is an estimate based on review of only 150 records.* *Exact follow-up and length of follow-up not clear. No information on time from hysterectomy to each event*. QS = 7
Piscitelli North Carolina, USA Retrospective cohort, case notes review 1995	**N = 697** Hysterectomy for benign disease and had vault smears 630 = had normal cervical smears pre hysterectomy 63 = abnormal smears pre-hysterectomy	Followed up by vault smears for an average of 13.7years. 1266 vault smears total (average 1.8 per patient)	**n1 = 33**: Slight atypia = 22, Mild dysplasia = 8, Moderate = 2, Severe = 1 25 were found at the initial examination (0.25-36yrs). 8 were found at a subsequent smear (2.25-45yrs) **n2 = 2** The extremely low incidence of vaginal carcinoma combined with the lack of evidence supporting the effectiveness of screening patients after hysterectomy suggests that less screening may be more desirable.	*One of the few papers where the stated aim was to determine the relevance of vault smear tests.* *Incomplete description of the frequency and reasons for vaults smears.* QS = 6
Videlefsky Atlanta, USA Retrospective cohort 1997	2066 identified as eligible, random selection of **N = 220.** with a hysterectomy for benign conditions and vault smears	All had one or more vault smears. 1,211 smears (range 1-21) Mean interval =19.5months. Mean time from hysterectomy to first smear was 13.2months (range 0 -	**n1 = 7**: 4 no intervention, 3 treated. Long-term, 6 had normal vault smears and 1 had atypical squamous cells of undetermined significance. 5 were from the 164 with previously normal histology. 2 from the 56.with previously abnormal histology. **n2 = 2**	*The use of routinely collected computerized records at one centre and the absence of active follow up of study participants indicates the potential for under ascertainment of subsequent events*. QS = 7.5

	164 = no prior cytological abnormalities 56 = prior abnormality: 12 - HPV induced changes / mild dysplasia 44 - moderate / severe dysplasia	155). Average duration of follow up 89 (3-175) months	**n3 = 0** Most routine vaginal cuff cytology screening tests need not be performed in women who have had a hysterectomy for benign uterine conditions. . . There are currently no known scientific benefits from routine vaginal cuff smear screening, and there can be possible risks associated with performing unnecessary procedures.	
Wiener South Glamorgan, UK Retrospective Cohort of women identified from, 'The Cardiff Cytology Study' 1992	**N = 195** women hysterectomy for pre-invasive disease of cervix (CIN or adenocarcinoma-in-situ). All had vault smears	143 = >10yrs follow up 95 = 15 years follow up 43 =>20yrs A total of over, 2,800 woman years followed up with vault smears	**n1 = 5:** in women who had CINIII originally, at 4, 4 and 20 months, 12 & 16 years **n2 = 3:** at 20months, 12 & 16 years **n3 = 1:** at 16 years having been lost to follow up. Cytological screening of all women who had a hysterectomy with a history of CIN is indicated for the first two years after hysterectomy. Thereafter the estimated incidence of 0.7 per 1,000 woman years is higher than the general population but it is not a sufficient reason to screen more frequently.	*Selection of and distribution of disease in the cohort is not adequately described. Events only occurred in cases with CIN III at hysterectomy but the proportion of the cohort with CIN III is not known. Apparently no review of eligibility of cohort. At least one sub-total hysterectomy is included which may increase the likelihood of observing abnormal smears.* QS = 4
Williams USA Retrospective case – control study 2000	9 HIV positive (cases) and 43 HIV negative women hysterectomised (controls) **N = 4** with cervical carcinoma in situ at hysterectomy and had vault smears	Controls were matched for diagnosis date, race and age Only 5 HIV positive patients complied with any follow-up	**n1 = 3** abnormal smears at an average of 12 months (6-24months) No recurrences in HIV negative controls Compliance with gynaecologic follow-up is very poor in this patient population . . . we continue to recommend treating HIV positive women in the same manner as their non-infected counterparts.	*Incomplete information on the follow up and characteristics of control group.* *Event rates in HIV positive women are unlikely to be generalisable.* QS = 5.5

* The term vault smears is used through the table instead of vault cytology tests as this was the accepted terminology at the time of publication.

Table 3i: Numbers of abnormal **vault smears** per study, grouped by histology at time of hysterectomy (QS ≥6)

Outcome	Author	Score	Vault Smear N	Events n	Benign n / N	CINI & II n/ N	CINIII n / N
n1 = Abnormal vault smears	Berget	7.5	237	4		0 / 8	2 / 206
	Fawdry	7.5	810	64			64 / 810
	Gemmell	9	219	9			9 / 219
	Kalogirou	7.5	793	210			210/793
	Pearce	7	5 682	79	79 / 5 682		
	Piscitelli	6	697	33	33 / 697		
	Videlefsky	7.5	220	7	5 / 164	2/ 56	
TOTAL n1 406 / 8 658 4.7%			**8 658**	**406**	117 / 6 543 **1.8%**	2 / 64 **3.1%**	285 / 2 028 **14.1%**

Table 3ii: Numbers of abnormal **vaginal biopsies** per study, grouped by histology at time of hysterectomy (QS ≥6)

Outcome	Author	Score	Vault Smear N	Events n	Benign n / N	CINI, II n / N	CINIII n / N
n2 = Dysplasia - biopsy proven	Berget	7.5	214	2		0 / 8	2 / 206
	Boyes	8	2 849	24			24 / 2 849
	Fawdry	7.5	810	12			12 / 810
	Gemmell	9	219	3			3 / 219
	Kalogirou	7.5	793	41			41 / 793
	Michalkiewicz	6.5	172	2		0 / 12	2 / 160
	Pearce	7	5 682	5	5 /5 682		
	Piscitelli	6	697	2	2 / 697		
	Videlefsky	7.5	220	2	1 / 164	1 / 56	
TOTAL n2 93 / 11 656 0.8%			**11 656**	**93**	8 / 6 543 **0.12%**	1 / 76 **1.3%**	84 / 5 037 **1.7%**

Table 3iii: Numbers of **invasive vaginal cancers** per study, grouped by histology at time of hysterectomy (QS ≥6)

Outcome	Author	Score	Vault Smear N	Events n	Benign n / N	CINI & II n / N	CINIII n / N
n3 = Invasive carcinoma	Boyes	8	2 849	0			0 / 2 849
	Fawdry	7.5	810	1			1 / 810
	Pearce	7	5 682	0	0 / 5 682		
	Videlefsky	7.5	220	0	0 / 164	0 / 56	
TOTAL n3 1 / 9 561 0.01%			**9 561**	**1**	**0%**	**0%**	1/3 569 **0.03%**

Table 4i: Benign histology at hysterectomy - summary of all events with time

Duration of Follow up	N = Fup by vault smears	Benign (events)		Recurrence Rate		Cumulative Rate		Notes n1 = abnormal smear n2= biopsy proven recurrence
Totals	**N = 7 318**	n1 = 117	n2 = 9	n1 = 1.6%	n2 = 0.12%	n1 = 1.6%	n2 = 0.12%	Miller, Pearce, Piscitelli, Videlefsky
Time Unknown	N = 6 457	5 682 79	7 154 8	1.4%	0.1%	79/5 682 1.4%	8/7 154 0.1%	Pearce, Miller
<1year	N = 861	861 2		0.2%		2/861 0.2%		Piscitelli & Videlefsky data Williams excluded as population too different from general population There were no cancers (n3), in this population.
1 – 2		858 4		0.5%		6/861		
2 - 4.9		854 4	162 1	0.5%	0.6%	10/861	1/162 0.6%	
5 - 9.9		850 7		0.7%		16/861		
10 - 14.9		844 6		0.7%		24/861		
15 - 19.9		838 11		1.3%		35/861		
20 - 24.9		668 0		0%		35/861		
25 - 29.9		668 1		0.1%		36/861		
30 - 34.9		667 1		0.1%		37/861		
35 - 39.9		666 0		0%		37/861		
40 - 44.9		666 0		0%		N/A	37/861	
45 - 49.9		666 1		0.1%		N/A	38/861	

Table 4ii CIN III Histology at hysterectomy, summary of all events with time

Duration of Follow up	N2 = Fup by vault smears n = events	CIN III			Notes n1 = abnormal smear n2= biopsy proven recurrence n3 = vaginal cancer
Totals	**N= 5 822**	n1 = 329 5.7%	n2 = 108 1.9%	n3 = 10 0.2%	Berget Boyes Fawdry Gemmell Halberg Hellberg Kalogirou Kirkup Liukko McIndoe'84 Michalkiewicz Weiner. Williams excluded as in Table 4i. Denominator data impossible to calculate from aggregate data thus columns omitted for clarity.
Time Unknown		287	8	0	
<1year		36	83	1	
1 – 2				3	
2 - 4.9		1			
5 - 9.9		3	12	1	
10 - 14.9		1	3	2	
15 - 19.9		1	2	3	

The electronic search strategies *Systematic review appendix A*

Searches that did not match any records when the main strategy was run (used for the Medline search) were simplified until matches were found, searches that produced a higher yield of matches were limited to human subjects and English language.

Medline (from 1966)

1. Vaginal smear OR vaginal vault smear OR Papanicolaou smear OR vault smear
2. Limit 1 to human AND English language

Embase (from 1980)

1. Vaginal smear OR vaginal vault smear OR Papanicolaou smear OR vault smear
2. Limit 1 to human AND English language

CINHAL (from 1982)

1. Vaginal smear OR vaginal vault smear OR Papanicolaou smear OR vault smear

CancerLit (from 1960)

1. Vaginal smear OR vaginal vault smear OR Papanicolaou smear OR vault smear

NHS Centre for Reviews and Dissemination, Database of Abstracts of Reviews of Effectiveness (NHSCRD – DARE)

1. Vault smear/All fields OR hysterectomy and smear/All fields

Turning Research into Practice (TRIP: from 1986)

1. Vaginal smear OR cervical smear OR hysterectomy

Cochrane Collaboration Database (all Databases and Registers included)

1. (VAULT and SMEAR) OR (VAGINAL and VAULT) OR (CERVICAL and VAULT) OR (HYSTERECTOMY and SMEAR)

Web of Science (WOS, 1981)

1. (Vaginal smear) OR (vaginal vault smear) OR (Papanicolaou smear) OR (vault smear)

VAULT SMEAR STUDY: ELIGIBILITY & VALIDITY FORM

Systematic review appendix B

REVIEWER :	**FIRST AUTHOR :**
REFERENCE ID :	**YEAR PUBLISHED :**
COUNTRY :	**Study Years :**

Have some women had a hysterectomy? YES n=

NO – *EXCLUDE*

(if n= is unknown, exclude)

Have some women been followed up by vault smear? YES n=

NO – *EXCLUDE*

(if n= is unknown, exclude)

Sample (ring all that apply) BENIGN CIN I CIN II CIN III INVASIVE

(*if only INVASIVE, exclude*)

Description of Study Population:

SAMPLE SIZE:

OUTCOMES? CANCER RECURRENCE OTHER _____

FOLLOW–UP? VAULT SMEAR COLPOSCOPY OTHER _____

DURATION OF FOLLOW– UP?

COMPLETENESS?

RESULTS:

If outcomes not directly attributed to population then EXCLUDE

AUTHORS CONCLUSION:

PTO - reviewers observations

Assessment tool (modified CASP) for assessment of cohort studies eligible for inclusion in the vaginal vault smears systematic review

Author & Identifier:				
Question **(score)**		**Yes** **(1)**	**No** **(0)**	**Don't Know (0)**
1	Are the aims clearly stated?			
2	Was an appropriate study design used?			
3	Do we know who exactly has been studied and was the population clearly described? (i.e. inclusion criteria, region, time frame, age, hysterectomy, histology)			
4	Was the cohort recruited in an acceptable way? (i.e. was there selection bias, does the cohort represent the study population, was everyone included that should have been)			
5	Was exposure accurately measured? (i.e. do we know if they had a hysterectomy and what was the histology at hysterectomy for whole cohort)			
6	Was follow up completely described? (i.e. duration and completeness)			
7	Did the numbers add up? (i.e. is everyone accounted for)			
8	Was outcome systematically measured? (i.e. same method for all women – is there a standard minimum done to assess all women, to minimize bias)			
9	Were the appropriate outcome measures? (i.e. histologically confirmed disease or recurrence)			
10	Have confounding factors been considered (i.e. HIV & HPV , accounted for in study design)			
	TOTAL SCORE			

Appendix B: An audit of ten years of vault cytology testing.

Vaginal vault cytology tests: Analysis of a decade of data from a UK tertiary centre

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Word count: 3,125

ABSTRACT

Objectives: To examine temporal trends in the use of vault cytology tests in primary and secondary care and the demographics of those women tested.

Methods: Retrospective analysis of routinely collected data concerning women who had a vault cytology test processed during a 10-year period (1 April 1995-31 March 2005), at Birmingham Women's NHS Foundation Trust.

Results: 8,457 vault cytology tests from 3,164 women (range 1-17 tests, median=2), were processed representing approximately 2% of the Department's cervical cytology workload. There was a significant reduction in annual numbers processed *(*Pearson correlation -0.958, $p<0.001$*)*. Significant abnormalities (mild dyskaryosis or worse) were detected in 4.5%, with malignancy being detected in less than 0.1%. The unsatisfactory cytology test rate was 10.7% overall.

There was a reduction in the numbers of vault cytology tests coming from the community, hospital outpatient clinics and operating theatres over time (χ^2 for linear trend=139.53, 9df, $P<0.0001$). Tests originating from community settings had lowest disease detection rates: no malignancies and only two severe abnormalities were detected from almost 4,000 primary care samples; abnormal results represented 2.8% (n=113), of which the majority (n=73) were borderline results. All cancers (n=8) were detected in samples taken in gynaecology and colposcopy clinics.

Conclusions: Vault cytology test usage appears to be reducing, particularly from out-patient clinics and primary care. Community detection rates are very low. Further research is required to establish the true costs and benefits of vaginal vault cytology.

MESH Keywords: Cervical screening, vaginal vault cytology, cervical cytology, clinical audit, Papanicolaou test.

INTRODUCTION

Hysterectomy is the most commonly performed major gynaecological operation and approximately 20% of women in the UK have had a hysterectomy by the age of 65. In England, around 40,000 operations are performed every year.[1] In the USA, a third of women have a hysterectomy, by the age of 65.[2] Benign indications (excessive bleeding, fibroids, prolapse, endometriosis, pelvic pain etc.) account for over 94% of hysterectomies. About 6% are undertaken either as a consequence of abnormal cervical cytology, cervical or other gynaecological cancer.[3]

Total hysterectomy includes removal of the cervix and leaves the vagina as a blind ending pouch. Subtotal hysterectomy, where a part, or all, of the cervix remains intact is an indication for continued participation in the cervical screening programme, however subtotal surgery comprises less than 3% of the hysterectomies in the UK.[4] Papanicolaou cytology tests of the vaginal vault (vault smears or, more correctly, vaginal vault cytology tests) are a means of detecting recurrent invasive or pre-invasive disease of the lower female genital tract in women who no longer have a cervix.[5]

Vault cytology testing may be undertaken on asymptomatic women who had no abnormal cervical pathology at hysterectomy, or prior to surgery, to screen for vaginal intraepithelial neoplasia (VaIN); VaIN being a precursor to vaginal cancer. However, VaIN is a hundred times less common than cervical intraepithelial neoplasia (CIN) and vaginal cancer is a rare malignancy with around seven cases per million women per annum.[6] Besides the presence of VaIN, the only group of

women who appear to be at increased risk of developing primary vaginal cancer are women whose mothers took diethylstilbestrol during pregnancy.[7]

Vaginal vault cytology tests fall outside the remit of the NHS cervical screening programme (NHSCSP), as they are not used to prevent cervical cancer. Recently the NHSCSP has confirmed that the call and recall system operated by primary care trusts will no longer be able to invite and recall women for vault cytology or record these results.[8] However, national guidelines currently make the following recommendations for women who have had a hysterectomy:

For women:

(i) on routine recall for at least 10 year prior to hysterectomy and no CIN identified at hysterectomy, no vault cytology is required;

(ii) with less than 10 years routine recall and no CIN at hysterectomy, vault cytology should be undertaken 6 months after surgery, with no further cytological follow-up if it is negative;

(iii) with completely excised CIN at hysterectomy, vault cytology should be undertaken at 6 and 18 months after surgery with no further cytological follow-up if both are negative;

(iv) with incomplete or uncertain excision of CIN, follow-up should be conducted as if the cervix were still in situ. [9, 10, 11]

Audit data suggested that too many vaginal cytology tests were being performed in South Birmingham, UK. Half were being undertaken in primary care with extremely

poor detection rates (only one serious abnormality was detected in almost 2,500 vault tests over five years).[12]

Very little data are available to inform estimates of the cost and benefits of routine screening, using vault cytology tests, for those women who had a hysterectomy for reasons other than cancer.[13] A survey of primary healthcare professionals demonstrated an inverse relationship between practitioners' perceived frequency of doing vault cytology tests and their level of knowledge about the test, with practitioner's knowledge generally being poor.[14] No routine data are collected about the frequency of screening using vaginal vault tests and in future it will be increasingly difficult to do so in view of the recent changes to recording.[8]

This study aimed to describe temporal trends concerning the use of vault cytology tests in both primary and secondary / tertiary care (the term secondary care is used hereafter to refer to all non-community based care). Its objectives were to describe which professionals were taking vault cytology samples, on whom and what the test results revealed.

METHODS

The pathology department and cytology laboratory, at the Birmingham Women's NHS Foundation Trust, has had computerised records since 1995. These include personal details of women, their clinical details, and results of all histological and cytological specimens processed.

Population:

All women who had one or more vault cytology tests processed during the period 1 April 1995 to 31 March 2005, at the Birmingham Women's NHS Foundation Trust were included. Vault cytology tests were identified by searching the local free text codes for the terms "VGSM" or "VGBR" (representing vaginal smear or vaginal brush samples), previous audits having confirmed this to be the most accurate indicator of cytology test type.[15] Complete cytology and histopathology records, including SNOMED codes and demographic data, were extracted for all eligible women. The cut off date of 31 March 2005 was chosen as the first point at which 10 years worth of electronic data became available but it was also only a few months after liquid-based cytology (LBC) was introduced to the department, on a rolling programme. Thus a small number of late samples may have been LBC but the vast majority were conventional.

Ethical approval was granted by South Birmingham Local Research Ethics Committee (9 November 2004 - 04/Q2707/234). Birmingham Women's NHS Foundation Trust provided R&D approval and NHS indemnity (Approval No 02020506, Project Ref WAD001).

Data handling and statistical analysis:

Data were fully anonymised before analysis. Vault cytology results were categorised as: unsatisfactory, borderline (equivalent to atypical), negative/normal, mild dyskaryosis (equivalent to low-grade squamous intraepithelial lesion), moderate dyskaryosis (including mild-moderate), severe dyskaryosis (moderate and severe equivalent to high-grade squamous intraepithelial lesion) and malignancy/cancer.

Due to ongoing uncertainty about the clinical significance of borderline results, this group was retained as a separate classification for most of the analyses. In summary statistics that describe 'all abnormalities', borderline results are included; where 'significantly abnormal' results are discussed borderline results are omitted. Sample takers were categorised as: general practice, other community based (all family planning services and genitourinary medicine), gynaecology outpatients, colposcopy, other outpatient clinics (including oncology), wards (test usually taken in the operating theatre but attributed to ward on which patient stayed), private practice. Data were processed using FoxPro 5.0, Excel and Access 2000 (Microsoft), and analyses undertaken using StatsDirect v2.6.3 and SPSS v12.0.1.

RESULTS

When duplicate entries were removed, there were 8,457 records of separate vaginal vault cytology tests during the study period (Table 1 and Flowchart 1) representing 3,164 different women.

Numbers of vault cytology tests per woman:

The number of vault cytology tests per woman ranged from one to 17, with 47% of women having one test and over 87% having five or fewer during the ten year study period, following an exponential decay pattern (mean=3.06, median=2, mode=1).

Age of women having vault cytology tests:

Age at vault cytology followed a near normal distribution (range: 17 to 95 years, median=52 years. mean=53, mode=49). The median age of women having vault cytology tests increased over time (Table 1, *Pearson correlation 0.922, p<0.001*).

Source of vault cytology samples:

General practice was the most common setting for vault cytology tests, followed by gynaecology outpatient clinics (Table 1, Graph 1). Private hospitals contributed 3% of vault cytology tests but it should be noted that consultants at these hospitals may have sent pathology samples to other laboratories for analysis and this figure may be an underestimate.

The source of vault cytology tests varied over time (Table 1, Graph 1) with a greater decline in GP, other community settings and outpatient clinics than from the colposcopy service (GP and community sources versus all other vault cytology tests: χ^2 for linear trend=4.8 (9df, P=0.028); ward, theatre and out patient tests versus all other settings: χ^2 (linear trend)=139.53 (9df, P<0.0001); colposcopy versus all other sources χ^2 (linear trend)=87.33 (9df, P<0.0001).

Trends over time:

Analysis was based on financial years (1 April - 31 March). There was a significant downward trend in total numbers of vault tests analysed each year (Table 1, Pearson correlation -0.958, p<0.001). During the study period the cytopathology department processed almost 400,000 cervical cytology tests.[16] The percentage workload that vault cytology represented fell from 2.81% in 95-96 to 0.9% in

2004/05 (χ^2 for trend= 545.9, P<0.0001). The total numbers of cytology tests, processed by the laboratory each year, fell from a high of 42,987 in 1995/6 to 34,798 in 2005/6 (Table 1).[16]

Cytology results of vault samples:

The vault cytology test results for each complete data year are summarised in Table 2. Abnormalities were detected in 8.9% of tests, with malignancy being detected in less than 0.1%. The unsatisfactory sample rate of 10.7% compares reasonably well with the cervical cytology unsatisfactory rate of 9.3% nationally in 2003-04[16] prior to the introduction of LBC throughout the UK, and favourably with the in-house unsatisfactory rate of 11.6% during the study period.

Significant abnormality (mild, moderate, severe, invasive) was reported in 4.4% of all samples**,** with invasion suspected in 0.1% (n=8). National figures for cervical cytology, for the last year of the study (2004-05)[16], suggest that these findings are somewhat worse than those for cervical screening where only 3.3% of tests give abnormal results (i.e. mild 2.1%, moderate 0.7% severe 0.5%, invasive 0.0%).

The eight tests indicating malignancy were performed on four women, one of whom had 14 vault tests taken during the 10 year study period, four of them indicating malignancy. The pattern of results suggests that not only were fewer tests being done, as the years passed, but that lower grade abnormalities were being detected.

Comparison of vault cytology tests in the primary and secondary care setting:

General practice and the community setting had particularly low detection rates for significant abnormality over the ten year study period: No malignancies and only two severe abnormalities were detected from almost four thousand vault cytology tests taken in primary care (Table 3, Flowchart 1).

Abnormal test results (i.e. borderline, mild, moderate, severe or malignancy) represented 2.8% (113) of the total, with the majority (n=73) of these being 'borderline' results; whereas for the hospital settings (clinics, wards and operating theatres) the proportion of abnormal test results was 14.5% (n=616). Table 3 demonstrates the results of the tests by setting. All the cytology results that indicated cancer (n=8, from 4 women) were detected in tests taken in gynaecology or colposcopy clinics and all the women were aged over 60. Of the 93 samples that demonstrated severe abnormalities only three were taken in the community setting. These 93 results came from 39 different women, with a range from one to 14 tests each, although, as one might predict, for each woman the results often varied over time, reflecting their ongoing treatment.

When comparing national findings for cervical cytology with our study findings[16] by the source of sample (Table 4), proportions of all grades of significant result were different in our population from that found in the general population: mild 1.5% versus 2.1%, moderate 1.8% versus 0.7%, severe 1.1% versus 0.5%. However, when the age group 50-54 yrs of women whose samples came from primary care were considered (the majority of our study population) the study results were very similar to national findings for cervical cytology (mild 0.8% vs 0.7%, moderate 0.2% vs 0.2% severe 0.1% vs 0.1%).[16]

DISCUSSION

There was a steady fall in the number of vault cytology tests processed each year, which was particularly noticeable from primary care and gynaecology outpatient clinics. The average age of women having vault cytology tests appeared to be increasing over time and the most significant abnormalities were, nearly all, detected in secondary care settings.

Anonymising the data prior to analysis meant that crosschecking outlying data was not possible. However, internal audits at the cytopathology laboratory enabled verification of histopathology data and the increasing, consistent use of the new unique ten digit NHS number reduced the possibility of failure to link cytology tests undertaken in the same women. This study used all the available data for the specified period thus reducing the potential for bias associated with selecting a subset of data. Clinical practice in this area may not be typical of other locations, however analysis of data over a 10-year period meant that a proportion of the clinical staff in both primary and secondary care changed (retirement or relocation) and there is no evidence to suggest that our findings are atypical. Another issue that arises from the use of a single centre is the representativeness of the catchment population. Birmingham Women's NHS Foundation Trust may not be representative of the wider UK population; however the hospital catchment area includes a wide spectrum of both ethnic diversity and deprivation, with some patients being referred to the tertiary centre for specialist management, and others for generalist gynaecology.

National guidance concerning use of vault cytology tests was updated in 2003; the interval between vault tests post hysterectomy for CIN changed from '6 and 12 months after surgery' to '6 and 18months' and the requirement for a woman to completed 10 years of cervical screening prior to hysterectomy added. Analysis of the data was not influenced by this change and, due to the long study period, we do not believe that this affected our findings.

It is possible that the inclusion of data from private patients could have skewed the results as that sector of the population may not be representative of the local population. However, private vault cytology tests represented less than 3% of the total workload and the results obtained were consistent with those from both primary and secondary care.

Nationally there was some variation in total numbers of cervical cytology tests performed annually over the study period; however, the net result was a very small drop in numbers, representing only a 1.3% fall over the decade of this study.[17] Locally, however, there was a significant drop in the number of cytology tests processed; 2004-05 represented the start of the move to LBC and implementation of the revised call/recall procedures in 2004 may also have had an impact, however these changes were not implemented fully until 2005-06.

The decline in the number of vault cytology tests during this period is far greater than the decline in the number of cervical cytology tests and cannot be explained by national or local trends. Within the 10-year study period research undertaken by the authors (2001-2003) may have increased primary care practitioners awareness about inappropriate use of vault cytology tests,[14] and may have contributed to the decline in vault tests undertaken in the community. In March

2002 a letter was sent to all GP surgeries in the area reminding smear-takers of national vault cytology test guidelines. These activities still do not explain the reduction in the number of vault cytology tests during the study period as the numbers had begun to fall in the period 1999/2000.

There were significant variations over the 10-year period in terms of slides being classified as inadequate for interpretation. This finding is likely to be multifactorial: in 1998-1999 the wooden Ayres spatula was withdrawn from use locally and the wooden extended tip Aylesbury spatula was adopted for 100% usage. Anatomically, the Ayres sampler was better suited to taking vault cytology tests than the Aylesbury and its introduction was associated with an increase in the classification of tests as inadequate.[18] Cytology tests became more difficult to read as blood and polymorphs obscured more of the field, this was particularly relevant to older women and those women undergoing vaginal vault cytology. At this time there was also more stringent application of the adequacy criteria for classifying a test as 'inadequate.[19,20,21] However, during the study period national inadequate sample rates varied from 4.5% to 17.5% of all submitted cytology tests, averaging 6.9% overall (excluding laboratories that were pilot sites for LBC at that time).[17] Birmingham Women's NHS Foundation Trust had one of the highest levels of inadequate rates in 2003-04. However, after the full introduction of LBC, which included formal training in the use of the Cervex-Brush, this level fell to 1.6% in 2005-06.[22] This change commenced in September 2004 but was phased in gradually and started towards the end of the study period so should not have had a substantial impact on these data.

According to national guidelines, vault cytology tests should be performed only on women who are at significantly higher risk of vaginal cytological abnormality than the general population of women having hysterectomy operations. Vault cytology is not funded as part of the national cervical screening programme and does not fit the criteria for a screening test as vaginal cancer is very rare. However, in this selected population of women having had a hysterectomy and then selected for vault cytology, thus defined by a clinician as being at higher risk, we found a very low rate of cellular abnormalities detected by vault cytology testing, with the vast majority of results being normal or of no clinical significance. Over 84% were classified as not demonstrating any significant abnormality, with a further 10.7% being unsatisfactory for interpretation. Of the 4.5% that did demonstrate a significant abnormality, most demonstrated either mild or moderate dyskaryosis (n=281). Severe dyskaryosis or invasive disease was reported in 1.2% of all the tests (101 from 8,457 tests) from 1.4% of the women (43 from 3,164 women).

These results suggest that vault cytology tests were probably not being restricted to higher risk women as they are similar to nationally detected findings from general cervical screening.[16] Thus, in our study population, this test appears to have low detection rates for disease. In particular, those tests being done in the community setting were unlikely to detect any significant abnormalities, thus raising questions about the usefulness of the vault cytology test in the community setting. Rates of high grade abnormalities did not increase over time, as the total number of tests was falling, which supports the hypothesis that the tests are not being restricted to higher risk women. This, raises the question of how VaIN and early

vaginal cancer are currently being detected and what role vault cytology testing now has.

In summary, it would appear that use of vaginal vault cytology tests is declining, particularly those taken in outpatient clinics and the community setting. This decline appears appropriate given the poor detection rates for significant disease in the community and that the call-recall system of the NHSCSP no longer includes women without a cervix. It is now timely to open discussions amongst clinicians as to how they can best detect and diagnose VaIN? What is the place for vault cytology? and is there a role for better training or education of clinicians who take vault cytology samples? To establish the true value of vaginal vault cytology tests it would be necessary to access more comprehensive data about women's screening histories, their hysterectomy pathology results and the results of any subsequent vault cytology tests and subsequent biopsies.

Acknowledgements: Thanks to Angela Ryan for her assistance during the design and setting up of the study, Ronan Ryan for his help in extracting data from Birmingham Women's Hospital database and Michelle Qume for her support with the statistical analysis.

Funding: Sue Wilson was funded by an NCCRCD Career Scientist Award during the period of this study. Helen Stokes-Lampard is funded by NCCRCD Researcher Development Award.

Author contribution: HSL, CW and SW conceived the study, HSL set it up and co-ordinated it. HSL and LB undertook the data extraction. HSL undertook the analysis and drafted the manuscript. All authors contributed to the final version.

Table 1: Trends over time in numbers of vault and cervical cytology tests and source of those tests

Year	Vault tests p/a	Change In vaults % p/a	Cervical tests p/a	Change in cervical % pa	% of workload as vaults	Odds ratios*	Mean age**	*Primary Care*		*Secondary Care*		
								GP	Community	Ward, & out-patients	Colp Clinics	Private
1995-96	**1,206**	N/A	42,987	N/A	2.81	1.00	51.97	550	22	589	45	0
1996-97	**1,032**	- 14.4	40,747	- 5.2	2.53	0.90	52.61	460	21	408	143	0
1997-98	**1,048**	+ 1.6	38,091	- 6.5	2.75	0.98	52.40	441	15	385	164	43
1998-99	**1,047**	0.0	38,829	+ 1.9	2.70	0.96	52.41	469	19	357	163	39
1999-2000	**986**	- 5.8	37,962	- 2.2	2.60	0.92	53.67	466	7	339	146	28
2000-01	**858**	- 13.0	36,615	- 3.5	2.34	0.83	53.14	370	8	292	154	34
2001-02	**734**	- 14.5	40,419	+ 10.4	1.82	0.64	53.91	*309*	5	245	133	42
2002-03	**671**	- 8.6	38,765	- 4.1	1.73	0.61	53.96	348	4	189	99	31
2003-04	**561**	- 16.3	36,963	- 4.6	1.52	0.53	53.71	289	0	147	101	24
2004-05	**314**	- 44.0	34,798	- 5.9	0.90	0.32	54.66	161	2	70	72	9
Total %	**8,457**	- %	386,176		2.19%		53.01	**3,863** 45.7 %	**103** 1.2%	**3,021** 35.7%	**1,220** 14.45	**250** 3.0%
								46.9%		*53.1%*		

* χ^2 for trend = 545.9, P<0.0001 ** Pearson correlation -0.922, p<0.001

Table 2: Variation in 'Results' codes over time

Result: Yr:	Non significant			Significant				Totals
	Unsatisfactory	Normal	Borderline	Mild	Mod	Severe	Cancer	
95-96 n	81	1,020	46	17	15	24	3	1,206
%	*6.7*	*84.6*	*3.8*	*1.4*	*1.2*	*2.0*	*0.4*	
96-97	77	876	39	9	16	13	2	1,032
	7.5	*84.9*	*3.8*	*0.9*	*1.6*	*1.3*	*0.2*	
97-98	82	879	28	17	23	19	0	1,048
	7.8	*83.9*	*2.7*	*1.6*	*2.2*	*1.8*	0	
98-99	81	877	43	11	22	13	0	1,047
	7.7	*83.8*	*4.1*	*1.1*	*2.1*	1.2	0	
99-00	128	761	53	15	19	8	2	986
	13.0	*77.2*	*5.4*	*1.5*	*1.9*	*0.8*	0.2	
00-01	111	656	57	11	18	5	0	858
	12.9	*76.5*	*6.6*	*1.3*	*2.1*	*0.6*	0	
01-02	65	598	37	13	17	4	0	734
	8.9	*81.5*	*5.0*	*1.8*	*2.3*	*0.5*	0	
02-03	129	484	32	12	9	4	1	671
	9.2	*72.1*	*4.8*	*1.8*	*1.3*	*0.6*	0.2	
03-04	109	401	33	10	8	0	0	561
	19.4	*71.5*	*5.9*	*1.8*	*1.4*	0	0	
04-05	39	241	12	10	9	3	0	314
	12.4	*76.8*	*3.8*	*3.2*	*2.9*	*1.0*	0	
Total	**902**	**6793**	**380**	**125**	**156**	**93**	**8**	**8,457**
%	**10.7**	**80.3**	**4.5**	**1.5**	**1.8**	**1.1**	**0.1**	
	95.5%			**4.5%**				

Table 3: Vault cytology results by source (1995-2005)

Result / Source		Unsatis factory	Normal	Border line	Mild	Mod	Severe	Cancer	Totals
General Practice	***N***	382	3,371	71	30	7	2	0	**3,863**
	%	(9.9%)	(87.3%)	(1.8%)	(1.0%)	(0.2%)	(0.1%)	(0%)	(100%)
	OR*	1	1	1	1	1	1	-	
Community	**N**	9	91	2	1	0	0	0	**103**
	%	(8.7%)	(88.3%)	(1.9%)	(1.0%)	(0%)	(0%)	(0%)	(100%)
	OR	0.9	1.0	0.9	1	-	-	-	
Subtotal	***N***	*391*	*3,462*	*73*	*31*	*7*	*2*	*0*	*3996*
GP/Community	***%***	*(9.8%)*	*(86.6%)*	*(1.8%)*	*(0.8%)*	*(0.2%)*	*(0.1%)*	*(0%)*	*(100%)*
Out patients	**N**	353	2,470	113	22	25	32	6	**3,021**
or wards	**%**	(11.7%)	(81.8%)	(3.7%)	(0.7%)	(0.8%)	(1.1%)	(0.2%)	(100%)
	OR	1.2	0.9	0.5	0.7	4.0	11.0	-	
Colposcopy	**N**	141	661	165	122	59	59	2	**1,220**
	%	(11.6%)	(54.2%)	(13.5%)	(10.0%)	(4.8%)	(4.8%)	(0.2%)	(100%)
	OR	1.2	0.6	7.3	10.0	24.0	48.0	-	
Subtotal	***N***	*494*	*3,131*	*278*	*144*	*87*	*91*	*8*	***4,241***
OPD / Colp	***%***	*(11.6%)*	*(73.8%)*	*(6.6%)*	*(3.3%)*	*(2.1%)*	*(2.1%)*	*(0.2%)*	*(100%)*
Private	**N**	17	200	29	2	2	0	0	**250**
	%	(6.8%)	(80.0%)	(11.6%)	(0.8%)	(0.8%)	(0%)	(0%)	(100%)
	OR	0.7	0.9	6.3	0.8	4.0	-	-	
Total		**902**	**6,793**	**380**	**125**	**156**	**93**	**8**	**8,457**
		10.7%	**80.3%**	**4.5%**	**1.5%**	**1.8%**	**1.1%**	**0.1%**	

** Odds ratios calculated compared with General Practice as a source*

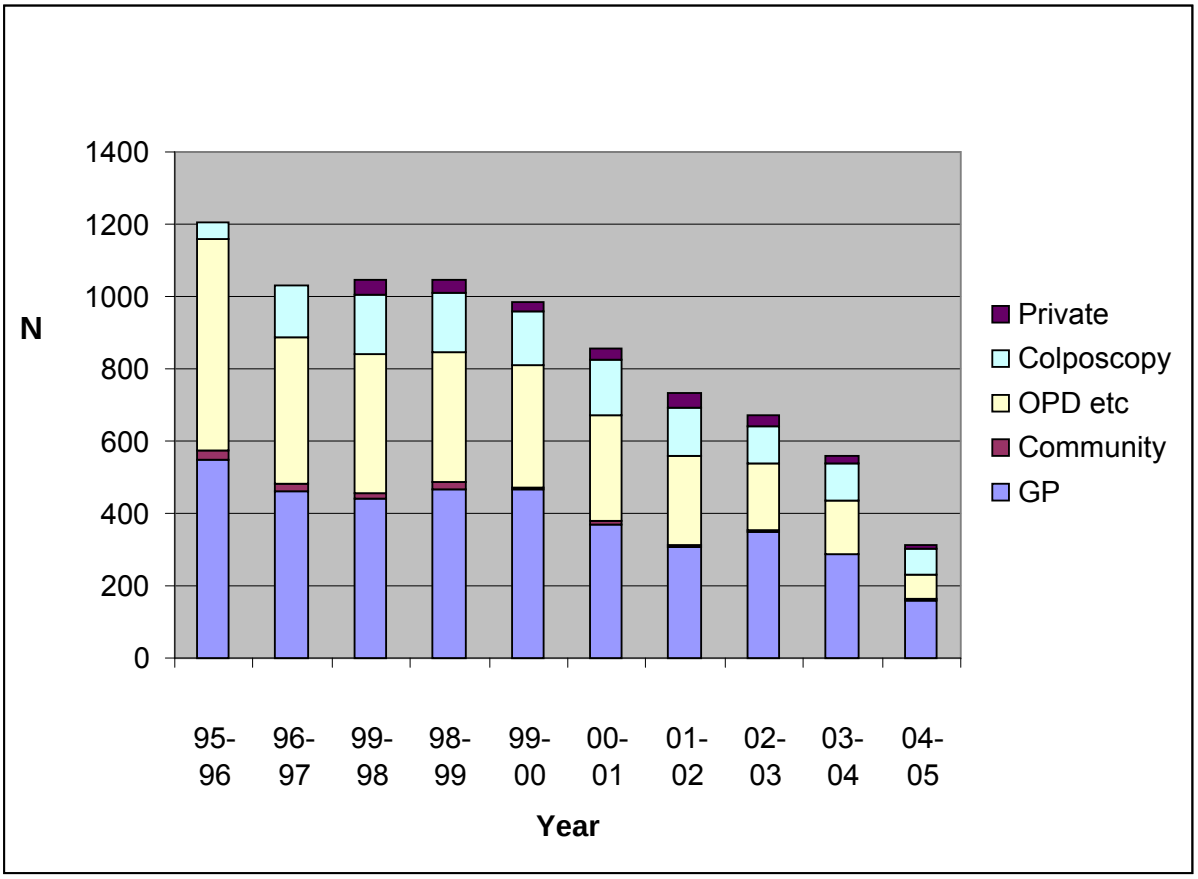
Table 4: Comparison of vault audit results with national cervical screening results from 2004/05 (percentages)*

	Mild	Moderate	Severe	Invasive
All ages / All sources				
Study results	1.5	1.8	1.1	0.1
National: all results	2.1	0.7	0.5	0
GP & Community				
Study results	0.8	0.2	0.1	0.0
National: all results	1.8	0.6	0.4	0.0
National: aged 50-54 only**	0.7	0.2	0.1	0.0
Hospital				
Study results	3.3	2.1	2.1	0.2
National: all results	6.8	2.5	1.9	0.1

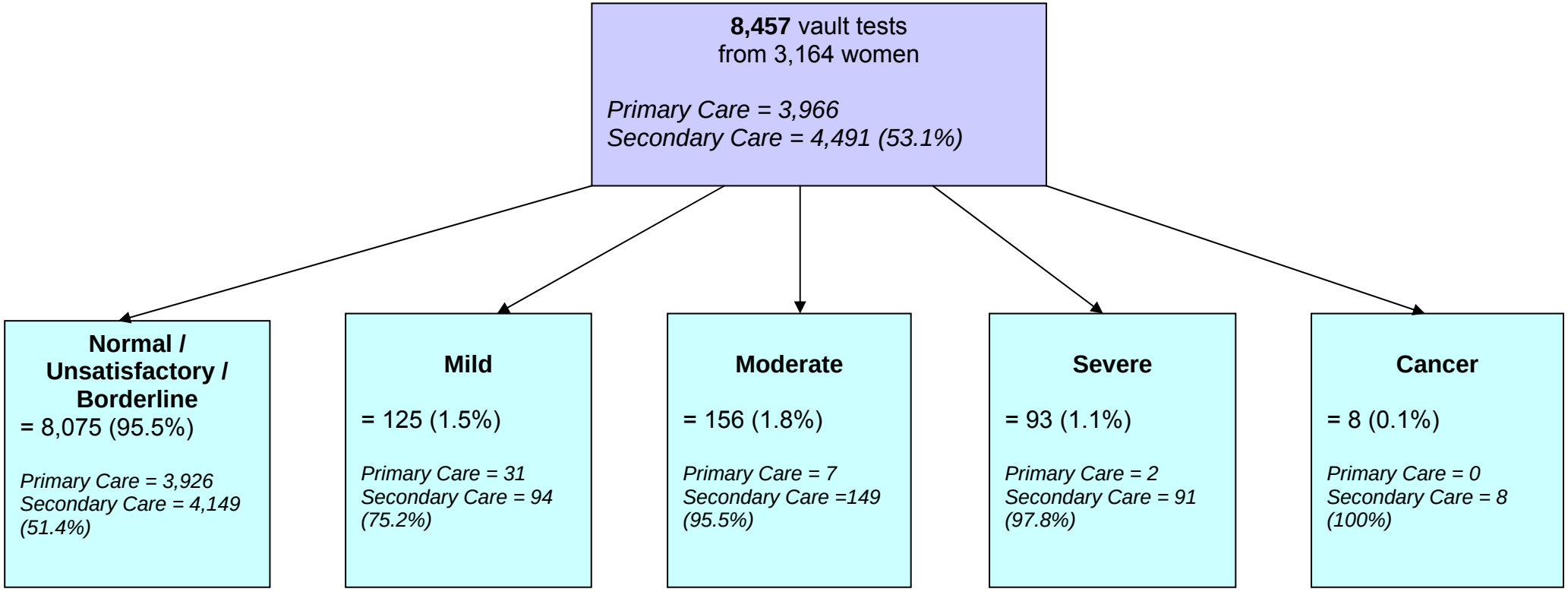
** National data taken from Table 14 of Cervical Screening Programme Bulletin: Samples examined by pathology laboratories, by source of sample and result of test 2004-05.*

*** Age specific data taken from Table 15 of Cervical Screening Programme Bulletin: GP & NHS Community Clinic samples examined by pathology laboratories, by result and age of women, 2004-05.*

Graph 1: Source of vault cytology tests, each year



Flowchart 1: Vault cytology tests data



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Appendix C Modulus 11 algorithm for NHS number check digit

The NHS number comprises 10 digits. The first nine are the identifier and the tenth is a check digit used to confirm the number's validity. The check digit is calculated using the Modulus 11 algorithm. There are four steps in the calculation:

Step 1: Multiply each of the first nine digits by a weighting factor as follows:

Digit Position (starting from the left)	Factor
1	10
2	9
3	8
4	7
5	6
6	5
7	4
8	3
9	2

Step 2: Add the results of each multiplication together.

Step 3: Divide the total by 11 and establish the remainder.

Step 4: Subtract the remainder from 11 to give the check digit.

There are two occasions where the check digit calculation process must be modified slightly:

- If the result of step 4 is 11 then a check digit of 0 is used
- If the result of step 4 is 10 then the number is invalid and not used

Example: Suppose the first nine digits of the number are 401 023 213

Step 1 - apply weighting factors

Digit Position	Value	Factor	Result
1	4 x	10	= 40
2	0 x	9	= 0
3	1 x	8	= 8
4	0 x	7	= 0
5	2 x	6	= 12
6	3 x	5	= 15
7	2 x	4	= 8
8	1 x	3	= 3
9	3 x	2	= 6

Step 2 – add the results of each multiplication together

40 + 0 + 8 + 0 + 12 + 15 + 8 + 3 + 6 = 92

Step 3 – divide the total by 11 (92 / 11) = 8, remainder 4

Step 4 – subtract the remainder from 11 to give the check digit 11 – 4 = 7

The complete new NHS number in this example is therefore: **401 023 2137.**

Appendix D to Appendix G

Not available in the digital copy of this thesis

Appendix H: Assumptions used in the WMQARC cervical screening status and history algorithms

Criteria (per woman)	Assumption
Women born before 01/10/1984 (aged 20 at first invitation)	Should attend for their first screen within 6 months of their 20th birthday OR within 5.5 years of the start of the NHSCSP (30/06/1993) - whichever is latest
Women born on or after 01/10/1984 (aged ~ 25 at first invitation)	Should attend for their first screen -2 / +6 months of their 25th birthday
Women aged 65 or over at diagnosis	Not eligible for screening at time of diagnosis **regardless** of any tests taken after the woman's 65th birthday
Women aged under 20 at diagnosis (born before 01/10/1984)	Not eligible for screening at time of diagnosis
Women aged under 24 10/12 at diagnosis (born on or after 01/10/1984)	Not eligible for screening at time of diagnosis
Women born before 01/01/1923	Have never been eligible for screening (regardless of whether they have attended for screening)
Criteria (per test)	**Assumption**
Tests taken on or after date of diagnosis	Always excluded from classification
Tests with private hospital sender codes	Always excluded from classification
Tests with a hospital sender code	Excluded from classification but recall number of months used if test is followed by a GP test recommending referral
Tests with normal recall or early recall action codes	Always included in classification regardless of intervals between tests
Tests taken before 01/01/1988	Always included in classification
Tests recommending referral	Only included in classification if taken at appropriate time interval after last test OR the test is the woman's first test and fits into criteria described
Tests taken when woman aged less than 24 10/12 (if born on or after 01/10/1984)	Excluded from screening status and screening history (there should not be any). Cases flagged as a QA issue
Tests taken when woman aged 65 or over	Excluded from screening status but are included in history
Number of months recommended recall	**Number of months assume woman should return for next screen**
36, 48 or 60	± 6
6 or 12	± 3
2 or 3	-1 and +3
1	Should not attend early, but can attend up to 3 months late.

Appendix J: Cancer and Gynaecological re-coding of ICD-10

#	Meaning of diagnosis codes	Relevant ICD10 Codes
01	*No interest to project**	*All else: A00-A50, A65-A99, B00-B20, B22-99,D50-D89, E-M,N: 0-64, N99, P, Q**
02	Neoplasms, malignant, non gynae	B21 (HIV) C00-C50, C60-C97
03	Neoplasms, in-situ, non gynae	D01-D05, D09
05	Neoplasms, benign non gynae	D00, D10-24, D29-D38, D40-D48
10	Obstetric general	O00, O10 - O99
12	Neoplasms, malignant gynae	C51-C58
13	Neoplasms, in-situ, gynae	D06-D07
14	Neoplasms, intraepithelial neoplasia, gynae	N87, N89.0-N89.3, N90.0-90.3
15	Neoplasms, benign & unknown, gynae	O01, D25-D28, D39
16	Other gynae diagnoses: Inflammation	N70 - N77
17	Other gynae diagnoses: Infection	A51-A64
18	Other gynae diagnoses: Bleeding, menstrual disorder and menopausal disorder	N91 - N95
19	Other gynae diagnoses NOS (Including endometriosis, prolapse, infertility, fistula, polyp, miscarriage)	N80-86, N88, N89.4-N90, N90.4-N90.9, N96-98, O02-O08
88	*Descriptive terms only (not true diagnosis), non gynae*	*R00 - Z99*
99	*Missing data (empty cells)*	-

**Items in italics represent codes that are not diagnosis based.*

Appendix K: Full re-coding of screening history before hysterectomy

Main Group	Full Code	Explanation	Conversion notes	
1	11	Index abnormal, previous history includes abnormal tests	Index abnormal *(borderline or worse):* 3rd digit =3/4/5	If 4th digit = 1, 5th digit = 4 **or** 4th dig 2/3/4/5/6 and 5th = 3
	13	Index abnormal, previous history only ever normal		If 4th digit = 1, 5th digit = 2 **or** 4th dig 2/3/4/5/6 and 5th = 4
	18	Index abnormal, previous history includes tests of uncertain significance		If 4th digit = 1, 5th digit = 3 **or** 4th dig 2/3/4/5/6 and 5th = 1/2
	19	Index abnormal, only one test pre-op		If 4th digit = 1, 5th digit = 1
2	31	Index normal, previous history includes abnormal tests	Index normal: 3rd digit=1	If 4th digit = 1, 5th digit = 4 **or** 4th dig 2/3/4/5/6 and 5th = 3
	33	Index normal, previous history all normal		If 4th digit = 1, 5th digit = 2 **or** 4th dig 2/3/4/5/6 and 5th = 4
	38	Index normal, previous history includes tests of uncertain significance		If 4th digit = 1, 5th digit = 3 **or** 4th dig 2/3/4/5/6 and 5th = ½
	39	Index normal, only one test pre-op		If 4th digit = 1, 5th digit = 1
3	81	Index of uncertain significance, previous history includes abnormal tests	Index uncertain *(inadequate or recall suspended):* 3rd digit=2/6	If 4th digit = 1, 5th digit = 4 **or** 4th dig 2/3/4/5/6 and 5th = 3
	83	Index of uncertain significance, previous history only ever normal		If 4th digit = 1, 5th digit = 2 **or** 4th dig 2/3/4/5/6 and 5th = 4
	88	Index of uncertain significance, previous history includes uncertain test results		If 4th digit = 1, 5th digit = 3 **or** 4th dig 2/3/4/5/6 and 5th = 1/2
	89	Index of uncertain significance, only 1 pre-operative test		If 4th digit = 1, 5th digit = 1
4	99	Never had any pre-op testing, or at least nil recorded in Exeter or too old to have ever been detected in programme (even if did have smears)	No index test	All 5 digit code where first digit is 1,2,9 **or** Any Single digit code starting 1,2,3,5,9

Appendix L: Published study protocol

Variation in NHS utilisation of vault smear tests in women post-hysterectomy: A study, using routinely collected datasets

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Abstract

Background

20% of women living in the UK have a hysterectomy during their lifetime, levels are higher in the USA, making it one of the most commonly performed major surgical procedures. Understanding of the indications for hysterectomy and of the rationale for follow-up of women post hysterectomy is currently limited. Guidelines concerning follow-up by means of vaginal vault cytology tests exist but these are not based on 'gold standard' evidence. Furthermore, the extent to which current practice reflects these guidelines is unclear. This study aims to determine the factors associated with variability in hysterectomy rates and subsequent follow-up after surgery by use of the vaginal vault smear cytology test.

Methods/Design

All women resident in the West Midlands region, of the United Kingdom, who had a hysterectomy operation between 1st April 2002 and 30th March 2003 will be identified from the Hospital Episodes Statistics database which also contains proxy data on deprivation status, derived from postcode and self declared ethnicity. These data will be linked to regional cervical screening records for each woman and histopathology laboratory records from the relevant hospitals. Study objectives are

to describe: Indications for the hysterectomy operation, histology at hysterectomy, subsequent follow-up by use or non-use of vaginal vault cytology tests and variation between histological groups. Additionally the data will be categorised according to a woman's cytology screening history prior to surgery (i.e. always normal, borderline, resolved abnormalities, CIN etc) and these different groups compared. Variations in these outcomes according to age, deprivation and ethnic group will also be examined. Analysis will be undertaken using SPSS.

Discussion

This study will clarify patterns of current practice in one large English region and determine whether this practice reflects existing guidelines. The study will also strengthen the evidence base for future guidelines.

Study registration: National Research Register N0138173331

Background

Surgical removal of the uterus (womb) is a ‘hysterectomy’ operation; over 98% women who have their uterus removed also have the cervix uteri or ‘neck’ of the uterus removed at the same time, a total hysterectomy[1]. This leaves the vagina as a pouch with a blind end at the site of amputation of the cervix. There were around 39,000 hysterectomy procedures undertaken in the UK in 2005 [2], a cumulative lifetime incidence of 20% [3, 4], making it one of the most frequently performed major surgical procedures [5].

The most common indication for a hysterectomy is menorrhagia which accounts for 46% of all hysterectomies. Prolapse accounts for a further 20%, and fibroids (or leiomyoma) another 18%-21% [6]; 90% of hysterectomies are performed for benign or noncancerous conditions [7].

Hysterectomy is inversely associated with social class and education with women from lower social classes being more likely to have a hysterectomy [3]. Several large cohort studies have examined the indications for hysterectomy in the UK, however none has published details of how these women are followed-up or the cost-effectiveness of the vaginal vault cytology test (known colloquially as a 'vault smear') in the population [3,4,6]. A vault smear is a cytological sample taken from the blind end of the vagina; the vault smear is used a means of identifying recurrent cervical cancer or the development of vaginal neoplasia. Total hysterectomy is usually a reason for ceasing recall from the routine cervical screening programme, as the cervix is no longer present.

No international consensus exists on the appropriate extent of cytological screening in women who have undergone hysterectomy, as evidence for the appropriate use of vaginal vault smears post-hysterectomy and the optimum period of follow-up is sparse. The majority of published studies recommend the use of vaginal vault smears in the follow-up of women who have had a hysterectomy subsequent to the diagnosis of an invasive tumour of the cervix uteri, or where invasive disease is an

incidental finding at hysterectomy [8,9,10,11,12]. A systematic review of the literature [13] could identify no robust controlled trials that establish the value of the follow-up, by vault smears, for women who have had a hysterectomy for benign indications. The available evidence does, however, suggest that the vault smear test has a very low positive predictive value when used as a screening tool in the absence of symptoms or clinical signs [8,9,14]. Therefore, most commentators recommend that vault smears for post-hysterectomy follow-up are only required for women who have had a histological diagnosis of Cervical Intraepithelial Neoplasia (CIN) III or frank malignancy [10,11,12]. Some go as far as to say that even in women with previous cytological abnormality, vault smears should be limited to those who present with symptoms or in whom an abnormality is detected clinically [15].

Currently the UK National Health Service Cervical Screening Programme (NHSCSP) guidelines for the use of vaginal vault smears are: [16,17]

(i) for women on routine recall for at least 10 years prior to hysterectomy, and no CIN in the histopathology sample at hysterectomy, no vault cytology is required.

(ii) for women with less than 10 years' routine recall and no CIN at hysterectomy, a sample should be taken from the vaginal vault six months after surgery and there should be no further cytology follow-up if it is negative.

(iii) for women with completely excised CIN at hysterectomy, a sample should be taken from the vault at 6 and 18months after surgery and there should be no further cytology follow-up if both samples are negative.

(iii) for women with incomplete or uncertain excision of CIN follow-up should be conducted as if the cervix were still in situ (i.e as for low and high risk follow-up).

(iv) women who have undergone a hysterectomy but where the cervix is not completely excised are treated as if the cervix were still present and as such they remain in the normal cervical screening programme.

In a survey of primary healthcare professionals in South Birmingham, UK, half of all vault smear tests were conducted in the primary care setting but primary healthcare professionals' knowledge about the role of the test was poor [18]. Professionals

whose knowledge about the test was best, performed the test least often, and only one significant abnormality was detected in over 5,000 vault smear specimens[18]. However, there is no recent reliable data on the patterns and variability in vault smear follow up and the extent of compliance with the national guidelines is unknown.

No large-scale population studies have been undertaken to establish the actual patterns of follow-up, by use of vault smear tests, after hysterectomy. One American study compared the results of vault smears with cervical smears, in matched controls, and noted that there was a significantly reduced risk of test abnormality in those followed up post-hysterectomy [19]. Vault smear tests undertaken in asymptomatic women can have a high false positive rate thus reducing the usefulness of the test[8]. Large-scale national cohort studies have reported on the socioeconomic distribution of patients undergoing hysterectomy [4] and the distribution of hysterectomy type (vaginal versus abdominal),[6] but none has examined the socioeconomic distribution of the histology results at surgery and the socioeconomic distribution of any subsequent follow-up by means of vault cytology.

No international consensus exists as to the most appropriate follow up by vault smear test after hysterectomy [18]; the UK guidelines are not based upon 'gold-standard' evidence [16, 17]. With the increasing pressure on diagnostic and treatment services, the evaluation of diagnostic services and identification of inappropriate testing are necessary prerequisites to improving the efficiency of service provision. Thus there is a need for an adequately powered, population based study to consider the issue of hysterectomy follow up, the outcome of which may be used to inform national guidelines and encourage the teaching of best practice.

<u>Key objectives:</u>

- Estimate age and socioeconomic specific incidence rates for hysterectomy, in the West Midlands.

- Describe indications for hysterectomy in West Midlands.
- Describe variations in incidence and establish those factors associated with variability.
- Establish the current pattern of follow-up after hysterectomy by means of vaginal vault cytology test.

Methods/Design

Study design: This retrospective population-based analysis of routinely collected data will link data, from three key sources and hence enable us to address the study objectives. Figure 1 illustrates the main stages of the study.

Hospital episode statistics (HES) is the national statistical data warehouse for England of the care provided by NHS hospitals and for NHS hospital patients treated elsewhere. It is the data source for a wide range of healthcare analysis for the NHS, Government and many other organisations and individuals. For this study HES will be used to identify the population of women having a hysterectomy during the 2002 - 2003 fiscal year (1 April 2002 - 30 March 2003). These women's cervical screening history records will be obtained from the local health authority cytology databases; complete records of cytology results for all women who have had cervical screening within a local catchment area, ten such areas cover the West Midlands Health Authority region. All these cytology databases use the same suite of software and contribute to national statistics to ensure uniform reporting. These data will be linked and pseudo-anonymised to just NHS number: A national, unique, ten-digit identifier that makes it possible to share patient information across the whole of the NHS) then supplemental data about specific diagnosis and laboratory advice will be added from hospital pathology laboratory records [20]. The dataset will be fully anonymised to ensure patient confidentiality.

Selection and exclusion criteria: The cohort will include all women resident in the West Midlands region who had a hysterectomy operation during the defined study period.

Population: The West Midlands conurbation of 5.2 million inhabitants covers a very diverse population: It includes urban, suburban and rural areas ranging from some of the most to the least affluent wards in the country [21]. This represents a 10% sample of the population of England and Wales, (11% of England) and has, on average, a similar age, sex and socioeconomic profile to the UK as a whole [22].

Black and minority ethnic groups make up 11.3% of the West Midlands population, however the range within the region is quite striking with the 'Birmingham' Local Health Authority recording 29.6% of persons classifying themselves as being of black or minority ethnic group (second only to London) but the 'Staffordshire Moorlands' Health Authority figure is only 0.7% [22].

Study methodology: The study depends upon the extraction of data, from three separate routinely collected datasets, which will then be combined into a relational database (Microsoft Access 2007) in a format suitable for analysis and fully anonymised. Table 1 summarises all the data items to be requested and those that will be used to facilitate data linkage between the three databases.

Data sources:

The Hospital Episode Statistics (HES) dataset is managed by Northgate Information Solutions and access to sensitive confidential information requires permission to be granted by their security and confidentiality advisory group (SCAG) [23]. It is from this database that hospital in-patient data will be extracted: Data about all hysterectomy operations will be requested and then categorised as ‘total’ and ‘sub-total’ hysterectomies with the sub-total operations being excluded after verification.

The NHS Information Authority (NHSIA) has control over the Exeter database: The NHSIA is a ‘special health authority’ formed in 1999, the ‘Exeter’ system or now, more correctly the ‘National Health Applications and Infrastructure Service’ (NHAIS) is an integrated suite of software used by all health authorities at a regional level for holding administrative details of patients on GPs lists and used to manage patient

registration, GP payments, breast and cervical screening programme [24]. The NHSIA will provide the following dataset: All women, residing in the West Midlands region and identified from the HES dataset, who have ever had a smear test (cervical or vaginal).

Currently there are 17 cytopathology units in the West Midlands region and over 20 units where hysterectomy operations are performed routinely. To obtain accurate data concerning the histology at hysterectomy, it will be necessary to access the histopathology records from some hospitals directly. Since 1995 all histopathology laboratories in the West Midlands have had stand alone, computerised databases of their clinical records and thus data extraction will not require access to patient case notes, just to the electronic histopathology and cytopathology records.

Once matching and merging of all three data sets is complete, all data will be anonymised to the level of unique study identifier, age at hysterectomy and deprivation index; thus NHS number, surname, date of birth and postcode will be replaced with less identifiable indices.

The whole project was registered on the National Research Register in December 2004 entry: N0138173331. The approvals of both Multi Research Ethics Committee (MREC) and Patient Information Advisory Group (PIAG), have already been granted (MREC - West Mids MREC Approval granted on 27th April 2005 Ref: 05/MRE07/27, PIAG Full approval - 7th March 2006 Ref: 4-05(e)/2005). SCAG of HES granted approval for access to their data on 11th April 2006, Ref: ET0693.

Ethical issues: This project justifies the use of confidential patient data because the likely benefits to society outweigh the implications of that transient loss of confidentiality. The outcome of this research may have significant implications for the general population of women thus it may be argued that it is in the public's best interests for the research to be undertaken. There is no intention to feed information back to the individuals involved or take any decision that affects them. There are no practicable alternatives to access patient data of this quality that would be of equal

effectiveness. Confidentiality has been planned from the outset of this study, and data will be anonymised as soon as is practicable after data validation has taken place.

Power calculation/justification of sample size:

This is a pragmatic sample of all women in the West Midlands Region who underwent a hysterectomy operation but sample size calculations were undertaken during protocol development to ensure the study will have sufficient power to detect important differences.

The key groups of women are specified by their histology result at the time of surgery (benign / cervical intraepithelial neoplasia (CIN) / malignant) as this determines their recommended follow up according to national guidelines. The data in Table 2 were used to provide the estimated proportions on the basis of previous research by the authors (Stokes-Lampard H, Wilson S, Waddell C, Bentley L, Vaginal vault smears: 10-years of data from a tertiary centre (Birmingham Women's Hospital NHS Trust), awaiting publication.)

Assumptions:

- 4,500 hysterectomies annually in West Midlands.
- 80% of hysterectomies undertaken for benign indications
- 10% for CIN
- 5% for cancer
- 5% will sub-total hysterectomies and excluded from analysis (approximately 225 cases excluded).

For the benign histology group, a sample of 1,800 women will be sufficient to estimate prevalence of follow up to within +/-1% (95% CI); for the CIN and cancer groups the estimate would be to within +/-4% (95%CI). Thus the expected sample should be more than adequate and does not need to be expanded further.

Analysis: Will be undertaken using SPSS for Windows statistical software, with queries in Microsoft Access 2003® used to produce descriptive data. A substantial amount of descriptive analysis of the data will be undertaken i.e. frequency distributions, cross tabulations and simple proportions, much of which will be amenable to visual formats.

Comparison of the whole study population with the West Midlands and England populations (2001 census data) with respect to Index of Multiple Deprivation [22], age, and ethnicity will be undertaken initially and the results tabulated. Then age-specific incidence rates (5-year age bands) for hysterectomy will be calculated.

Pre specified analysis will be used to describe and explore those factors potentially affecting variability within the three main research areas i.e. i. Indications for hysterectomy, ii. duration of hospital stay after hysterectomy and iii. follow up after hysterectomy by means of the vaginal vault smear cytology (vault smear test),

Hospital diagnosis (obtained from HES records) will be used as a proxy for indication for hysterectomy. Indications for hysterectomy will be explored with respect to deprivation score, age, ethnicity and hospital where surgery took place. Duration of hospital stay will be described and explored with respect to age, ethnicity and deprivation score. Each of these will be considered further by histology type; benign, CIN (further subdivided into CIN I, II & III) and malignant. Pre-hysterectomy cervical cytology data will be explored with respect to age, deprivation and ethnicity. This data will be coded according to 'per protocol' and 'non-protocol' patterns, according to UK guidelines, using an algorithm constructed by the cancer registry in the West Midlands, this is to ensure standardised results to facilitate future analysis. Post-hysterectomy vault cytology will be explored with respect to age, histology type, deprivation and ethnicity. Most of this descriptive analysis will be explored using χ^2 and t-tests as appropriate.

Multiple regression analyses will aim to determine the relative importance of those factors (i.e. age, deprivation index, hospital of procedure and ethnicity) on the outcomes of interest.

Finally, differences in the rates of vault smear cytology between the different histology sub-groups will be further explored using Kaplan-Meir survival analysis. The sub-groups will be compared with national guidelines to establish compliance.

Outcome measures:

- Hysterectomy rates: Age and deprivation index standardised rates; histology, consultant and unit specific rates.
- Proportion of women who have smear tests that undergo a hysterectomy procedure by histology and also by age, deprivation index, hospital and indication for surgery.
- Proportions of those women having a hysterectomy which results in the histology being reported as benign / CIN / malignant.
- Proportion of those having a hysterectomy that are followed up by vault smear tests, with respect to histology group (benign / CIN / malignant), age, deprivation index, hospital, origin of test (primary or secondary care) consultant and indication for surgery.
- Analysis of over / under use of vaginal vault smears with respect to current national guidelines.

Discussion

Pilot work suggests that too many vault smear tests are probably being undertaken and that this test has poor sensitivity to detect disease in low risk women. These findings fit with some published work but there is a dearth of high quality research in this area.

This research will establish which women are currently having hysterectomy operations and determine when vault smear cytology tests are being done, both in terms of time elapsed post-operatively and histological indication for the test. Thus, compliance with current guidelines will be established and evidence to support the development of future guidelines will be generated.

Abbreviations

Hospital Episode Statistics = HES. Multi-Centre Research Ethics Committee = MREC. Patient Information Advisory Group = PIAG. Papanicolaou smear test = Pap test. Date of Birth = DOB. National Health Service Cervical Screening Programme = NHSCSP. Cervical Intraepithelial Neoplasia = CIN
Security and Confidentiality Advisory Group of HES = SCAG. NHS Information Authority = NHSIA.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

HSL and SW conceived the idea for the study, JM advised during the protocol development. HSL will be undertaking the research with SW and JM providing supervision and statistical expertise. HSL wrote the first draft of this manuscript but all authors have contributed to and approved the final version.

Acknowledgements

Helen Stokes-Lampard, Sue Wilson and John Macleod are all funded by awards from the National Co-ordinating Centre for Research Capacity Development, Helen Stokes-Lampard is the recipient of a Researcher Development Award, Sue Wilson and John Macleod are both recipients of Primary Care Career Scientist Awards.

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Figure 1: Study design

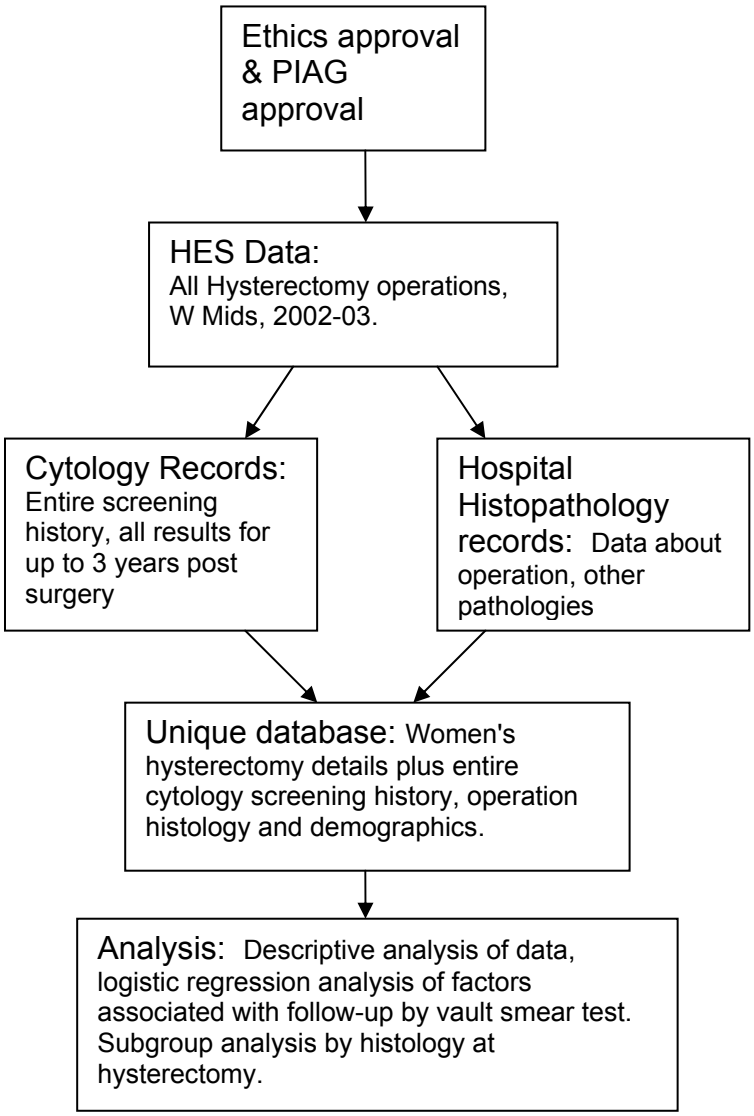

Table 1: Summary of extracted data and derived data items to be obtained from the three sources.

	Hospital Episode Statistics (HES)	**'Exeter' Cervical Screening data**	**Local Hospital Histopathology data**
Identifiers for linkage	NHS Number, date of birth, postcode of home address.	NHS Number, date of birth, postcode of home address.	NHS Number.
Data items	Ethnicity, dates of hysterectomy operation, admission and discharge, surgical operation code(s) OPCS, diagnosis code(s) SNOMED morphology, hospital, consultant, GP and PCT of residence.	Dates of all smear tests, results of those smear tests and recommended follow up, details of smear taker, registered GP, current cervical screening status and date of death (where applicable).	Details of histology at hysterectomy, details of all specimens removed, details of results of analysis (morphology or diagnosis codes), full details of smear tests processed at the laboratory.
Data to be thus derived or calculated	Deprivation score (IMD), duration of stay, diagnostic grading of operation (benign vs pre-malignant or malignant disease), age at surgery.	Deprivation score (IMD), scoring of screening history using algorithm, whether any vault smears undertaken (also using operation date from HES).	Confirmation of whether total or subtotal hysterectomy undertaken.
Explanatory Notes	Request full data on all West Midlands resident women who had a hysterectomy during the year, 1st April 2002 to 30th March 2003. Requires approval of HES security and confidentiality advisory group.	Request full cervical screening histories on all women identified in HES database. Requires individual permission from each of 10 database controllers.	Request full histopathology records on all women with NHS numbers identified in HES. Requires permission from each of 17 hospitals ethics committees and heads of department.

Table 2: Estimated numbers of women in each histology category

	Sub-Total (Excluded)*	**Benign**	**CIN**	**All Cancers**	**Totals**
Not followed up VS	*N/A*	3240 90%	90 20%	23 10%	3,353
Followed-up VS	*N/A*	360 10%	360 80%	202 90%	922
Totals	*225* *5%*	3600 80%	450 10%	225 5%	**4,275 (95%)***

* with 5% excluded for being sub-total operations.

Appendix M: Details of dissemination

BACKGROUND WORK TO THIS STUDY, BY THE AUTHOR

1. Questionnaire Survey

Publications in Peer reviewed journals

- **H J Stokes-Lampard**, S Wilson, T Allan, C Waddell, S Kehoe. Vaginal vault smears –'know more – do less' a questionnaire survey of primary healthcare practitioners. *Cytopathology* 2005,**16**,5,244-52.

Conference Proceedings

- **H J Stokes-Lampard**, S Wilson, C Mann, T Allen, S Kehoe, C Waddell, L Grovesnor. Vaginal Vault Smears – Use and abuse in Primary Care. Parallel plenary session. Nov 2003, UKFPCRN, Birmingham, UK
- **H J Stokes-Lampard,** S Wilson, C Mann, T Allen, S Kehoe, C Waddell, L Grovesnor, R Todd. Vaginal Vault Smears, are we doing them too often? Parallel plenary session. November 2002, NAPCRG, New Orleans, USA.
- **H J Stokes-Lampard**, S Wilson, C Mann, T Allen, S Kehoe, C Waddell, L Grovesnor, R Todd. Vaginal Vault Smears – When, Where & Why? Parallel plenary session.. July 2002, SAPC, Birmingham, UK

2. Systematic review of literature concerning the use of vaginal vault smear tests

Publications in Peer reviewed journals

- **Stokes-Lampard H**, Wilson S, Waddell C, Ryan A, Holder R, Kehoe S. Vaginal vault smears after hysterectomy for reasons other than malignancy: a systematic review of the literature. *BJOG* 2006; 113:1354-1365.
  (Appendix A includes main results table)

Conference Proceedings

- **H J Stokes-Lampard** et al: Vaginal vault smears, a systematic literature review and analysis of their usage after hysterectomy for indications other than invasive cancer. October 2006 NAPCRG Tuscon, Arizona, USA. Parallel plenary
- (Best Plenary of Conference prize winner): **H J Stokes-Lampard**, S Wilson, C Waddell, S Kehoe, A Ryan, L Grovsenor, T Allan, R Holder, R Ryan. Vaginal Vault Smears – An overview of their use (Incorporating: A systematic review of the literature, a questionnaire survey, and an audit of current practice). BSCCP 30 March – 1st April 2006, London. Plenary.

3. Hospital Audit

Publications in Peer reviewed journals (in press, see Appendix B)

- H Stokes-Lampard, S Wilson, C Waddell, L Bentley. Vaginal vault cytology tests: Analysis of a decade of data from a UK tertiary centre.

Conference Proceedings

- (Invited Plenary) **H J Stokes-Lampard**. Follow-up after hysterectomy, a record linkage study. NIHR National Trainee Conference, Birmingham 18 September 2007.
- **H J Stokes-Lampard**. Disentangling the data: An analysis of 10 years of histopathology records from Birmingham Women's Hospital NHS Trust. UKFPCRO 27 Nov -28 Nov 2006, Liverpool.

DISSEMINATION OF CURRENT STUDY FINDINGS TO DATE

Peer reviewed journals

- **Study Protocol (Appendix L): H J Stokes-Lampard**, J Macleod, S Wilson, Variation in NHS utilisation of vault smear tests in women post-hysterectomy: A study, using routinely collected datasets BMC Women's Health 2008, 8:6. http://www.biomedcentral.com/content/pdf/1472-6874-8-6.pdf

Conference proceedings

- **H Stokes-Lampard, J** Macleod, S Wilson Who is having a hysterectomy operation and are they being followed up appropriately? Variation in NHS utilisation of vaginal vault cytology tests in women post-hysterectomy. SAPC Annual Conference. 8-10th July 2009, St Andrews, UK.

Conference posters

- **H J Stokes-Lampard**, J Macleod, S Wilson. Which women are having hysterectomy operations and are they being followed up appropriately? Factors associated with variability in NHS utilisation of vaginal vault cytology tests in women post-hysterectomy; a data linkage study. RCGP National conference, 4-7th November 2009, Glasgow, UK.

- **H J Stokes-Lampard**, J Macleod, S Wilson. Which women are having hysterectomy operations and are they being followed up appropriately? Factors associated with variability in NHS utilisation of vaginal vault cytology tests in women post-hysterectomy; a data linkage study. NIHR Award holders conference, 22-23rd September 2009, Manchester, UK.

- **H J Stokes-Lampard**, S Wilson, J Macleod. Factors associated with variability in NHS utilisation of vaginal vault cytology tests in women post hysterectomy: Early results from a data linkage study (a work in progress). BSCCP Birmingham, 9-10th April 2008. (Awarded a prize for Best Abstract).

FURTHER PLANNED DISSEMINATION OF CURRENT STUDY FINDINGS

- **H J Stokes-Lampard**, S Wilson, J Macleod, R Holder. Follow-up after hysterectomy by vaginal vault cytology: a database linkage study of women having a hysterectomy operation in the West Midlands 2002-2003. *(Full research paper).*

- **H J Stokes-Lampard**, S Wilson, J Macleod, R Holder. A socio-demographic analysis of the cohort of women having a hysterectomy in the West Midlands 2002-2003. A database linkage study. *(Full research paper).*

- **H J Stokes-Lampard**, J Macleod, S Wilson. Researcher beware: potential pitfalls of data linkage studies using routinely collected hospital histopathology laboratory data. *(Editorial).*

- **H J Stokes-Lampard**, J Macleod, S Wilson. Which women are having hysterectomy operations and are they being followed up appropriately? Factors associated with variability in NHS utilisation of vaginal vault cytology tests in women post-hysterectomy; final conclusions from a data linkage study. *(will be submitted as an international conference presentation or poster to SAPC, NAPCRG, RCGP, BSCCP, in addition to presentation at various regional meetings).*